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THE AMERICAN
JOURNAL OF PHARMACY

APRIL, 1919

EDITORIAL.

THE EVIL OF DISPARAGEMENT.

The idealist, who by legitimate arguments and methods seeks to improve the practices of his vocation, deserves praise and encouragement. The higher his aim, the more ethical his purpose, the greater the possibility of a measure of success. He performs a service of value not alone to his chosen sphere of activity but also in that general advancement that we designate as the progress of the world.

The true idealist is naturally an optimist and, appreciating the value of the efforts of his predecessors, he predicates the advances that he advocates upon the foundations that they have established By his very efforts in behalf of professional idealism, he evidences that he realizes that the goal is still in the distance and far ahead. The thinking observer is convinced that the desired purity of practice is not universally observed in any of the professions; that professional idealism is not now extant and that this is still an ethical ignus fatuus. The frailties of the human race and the perversities of human minds are continuously cropping out and attempting to demolish the work of the idealist. The several professions are cursed by their shysters, their quacks, and their hypocrites who shatter the ideals. The philosopher knows full well that all professional advancement will be the fruit resulting from the cultivation of the idealists.

In marked contrast to the services of the true idealist are the efforts of the false idealist, the disparager. He develops pessimism and with a deranged vision obstructing a view of the progress already made in his vocation, he endeavors to present his distorted picture and mental aberration to his associates. He may even hold

aloft the banner of professionalism while applying thereto the torch of disparagement.

Applying specifically our comments to the domain of pharmacy and especially American pharmacy, current literature demonstrates that it has become quite the fashion for a coterie of self-styled leaders who are possibly "rich in words and ideas but poor in the true knowledge and genuine studies," to continuously and deliberately "knock" pharmacy in print and in public utterances and some of the issues of "pharmaceutical journals" have been loaded down with disparagements of pharmacy.

Constructive criticism is always welcomed by those having at heart the welfare and progress of their vocation. There is, however, a wide difference between a "boost" and a "knock" and this is the fundamental difference between idealism and disparagement. It is manifestly unfair and unjust to lay at the door of pharmacy all of the pernicious results of that deep-rooted evil in the practice of the various branches of medicine, selfish commercialism. The service of the pharmacist being the last stage in the medical attention, it is influenced by the methods of practice in vogue by his predecessors. It is evident, that the commercial status of pharmacy, that is so energetically decried, results very largely from the existing commercialized practice of medicine. The encomiums of the professional status of the practice of medicine that are indulged in by some of the contributors to the pharmaceutical press are certainly not in harmony with the criticisms and deserved condemnations of medical practices published in recent issues of the *Journal of the American Medical Association.*

Let us recognize that "service is the base of all worthy enterprise." The pharmacist who conscientiously renders the service demanded of him by the community in which he is engaged and the status of the medical practice therein, is properly filling his responsibility to his profession and his duty to his fellow men.

Even a hasty review of the history of the development of pharmacy in America presents a long list of names of pharmacists who, notwithstanding their practical service with the mortar and pestle and graduate, have applied their minds and pens to the advancement of the profession of pharmacy and the construction of its literature, and of those active at the present time, many either are, or have been, engaged in the duties of the apothecary. American pharmacy has no need to apologize for its professional evolution.

It is doubtful if the authors of disparagements often give any thought whatever to the influence of their adverse criticisms. Their reflections are not very creditable to the teachers in the pharmacy schools who for several generations gave their lives and services to the elevation of the profession nor to those of the present generation who are continuing their effort. How can pharmacists expect to gain the respect of others so long as pharmacists do not respect their own position in society? How can pharmacy hope for the dignity and recognition from the other professions when in its own societies and journals the claims to such are discredited? How many promising youths with laudable ambitions for professional careers have been driven from pharmacy by these disparagers? The importance of pharmacy to the nation has even been minimized before the departments of the government by unnecessary and uncalled for slurs.

No nation can exist for any length of time when the love of country and patriotism is destroyed. No municipality can develop into an industrial, commercial or educational city of importance where civic pride is lacking. Similarly no vocation, either trade or profession, can expect satisfactory, progressive elevation without pride in its accomplishments and whole souled support of its votaries. Pharmaceutical progress demands rational constructive criticism, a change in tack, and adherence to a chart devoid of disparagements.

G. M. B.

THE REVENUE BILL OF 1918.

After months of debate, discussion and conference the Revenue Act of 1918 was enacted by Congress and by Presidential approval became operative on February 25, 1919, and while some of its tax provisions are made operative at fixed dates thereafter the main feature, namely the income tax which again commits the Federal Government to an extensive system of direct taxation, is retroactive.

By amending the title of the Bill by the addition of the phrase "and for other purposes" Congress legalized the introduction of radical legislation entirely foreign to the main purpose of the measure. The question of prohibition, with its recurring battles between the "wets' and the "drys" should have been fought out in some other way than by the introduction of "jokers" and questionable legislation in such an important measure as the main revenue law.

Likewise, was it a vicious and unfortunate piece of legislation to introduce therein amendments to the Harrison Anti-Narcotic Act. Anti-narcotic legislation was never intended to produce revenue, but its purpose was and is to suppress the evil use of narcotics. This is purely a police duty and the enforcement of such laws should be placed in the Department of Justice and not in the Treasury Department.

In the past, on several occasions, we have plainly presented in these columns the fact that "the Departments of the Government Need the Advice of the Drug Trade." The bill now commented upon, again very forcefully illustrates such need and some of the provisions now enacted, which are not very creditable to an intelligent law-creating body, could have been eliminated or corrected if Congress had not heedlessly refused to accept the suggestions and advice of men fully acquainted with conditions and the drug trade practices, whose services and counsel were proffered.

Following the erratic views shown in the revenue enactments of Congress, the drug trade has again been singled out for special taxation and the products usually sold by the drug trade, not excluding needed medicines and the ingredients thereof, bear a heavy burden of taxes. Consequently the druggists must become acquainted with those provisions of the Act that relate especially to the articles that enter into their dealings. This is going to be a difficult task for the drug trade, and the more one studies the ambiguous language of the sections relating to these matters the more numerous become the uncertainties and the questions as to the proper actions under the law.

The interpretation of the law has been largely left to the officials of the Bureau of Internal Revenue and they have the grave responsibility of framing regulations for the administration of a law the language of which in many parts is so involved that the very intent of the law-making body is in doubt. With the most painstaking and conscientious efforts on the part of officials and merchants alike there will remain numerous pitfalls and innumerable possibilities for errors and misunderstandings.

The collectors of internal revenue of the various districts have issued notices calling attention to the provisions of paragraph 12, section 1001, which provides that persons carrying on any of the branches of the liquor business named, including the *retail liquor dealer,* under which class many of the retail druggists by the neces-

sity of complying with the revenue laws were registered, would be required in prohibition localities to pay a special tax of $1,000 and that "this section will prohibit the filling of prescriptions of distilled spirits in such territories unless $1,000 tax is paid." It would have been equally appropriate for these collectors to have added, that the payment of the $1,000 did "not exempt any person from any penalty or punishment provided by the laws of the states, territories or municipalities," or "authorize the commencement or continuation of any business contrary to such laws." This is one of the "jokers" introduced in the bill in the prohibition struggle and it is inconceivable that the ethical practice of medicine and pharmacy should be interfered with by such impractical legislation, and that professional efforts to conserve life and health could be so "juggled" by radical extremists with congressional sanction. It behooves the medical and pharmaceutical societies conjointly to see that in all state laws and municipal ordinances there is incorporated a properly worded exemption clause that will permit of the prescribing and dispensing of distilled spirits and wines in the legitimate exercise of their professional services.

Section 630 provides that after May 1, 1919, there shall be paid by the purchaser to the vendor at the time of sale, one cent for each ten cents or fraction thereof paid for any soft drink, ice-cream, ice-cream soda, sundae, or similar article of food and drink. The wording of this section, simple as the subject may appear, opens up at least two questions that may require official decisions and regulations to be promulgated. The wording of the section reads "when any of the above are sold on or after such date for consumption in or in proximity to such place of business." It would thus appear that if the *sale* is made prior to May 1, 1919, the *delivery* may be made at any subsequent time and be exempt from payment of the tax. Moreover, the tax need not be paid if the article is consumed elsewhere than on the premises of the vendor or in proximity thereto. Presumably the tax was to be levied upon this class of articles as luxuries and they cease to be such luxuries if bought and paid for in April or if consumed elsewhere than at the place of purchase. That such a ridiculous extension of the definition of a luxury, that such a gem of crudity, should be incorporated in an act of the United States Congress is as mortifying as ludicrous.

The drug trade had quite generally assumed that the tax on perfumes, toilet articles, etc., and on proprietary medicines was to be

a straight four per cent. tax on the wholesale price of these commodities instead of the two per cent. tax provided by the previous revenue bill, and that this was to be payable by the producer as heretofore in monthly reports. Section 907 of the Act, however, presents the possibility of an entirely different construction and a radical change not only in the rate of the tax to be paid on such articles when *sold on or after May 1, 1919, for consumption or use.* but also in method of payment. The tax to be imposed is "1 cent for each 25 cents or fraction thereof of the amount paid."

The method of collecting the tax imposed by this section is left to the judgment of the Commissioner and he is empowered to select either the collection "(1) *by stamp affixed to such article by the vendor, the cost of which shall be reimbursed to the vendor by the purchaser; or* (2) *by payment to the vendor by the purchaser at the time of the sale,* the taxes so collected being returned and paid to the United States by such vendor in the same manner as provided in section 502" (monthly returns under oath and in duplicate). The information available at present, is that the construction placed upon this section by the Department is that it is intended to be "a consumption" tax and *shall be paid by the purchaser.* The Canadian system of taxing proprietaries appears to have been in mind, and it is most likely that this tax will be collected by the affixing of a special stamp. The rate will be four per cent. on articles selling for 25 cents or more and ten per cent. on those selling for 10 cents and twenty per cent. on those selling for 5 cents. Under these conditions the salvation of the druggist or other vendor of such commodities will be in strict adherence to the intent of the law to make this a "consumer's tax," and to affix the stamp and collect the price from the purchaser with each sale.

It is to be noted that paragraph 2, relating to proprietary medicines, which are named by class designations, distinctly states that serums and anti-toxins are not to be included with the articles taxed as proprietaries. This is in conformity with a recent decision of the Commissioner of Internal Revenue, Daniel C. Roper, that vaccines, serums and similar biological products were not intended to be taxed under the revenue law of 1917, and the same decision will undoubtedly follow regarding the present law.

It is also noteworthy that toilet soaps and toilet soap powders have been excluded from the toilet articles, perfumes, etc., taxed under this section, and have been named in Section 900 under the

special tax of 3 per centum of the price at which they are sold by the manufacturer. It is assumed that under the title of toilet soaps and toilet soap powders will be included shaving soaps and shaving soap creams, and on these the tax will most likely be "absorbed" by the manufacturers or at least paid at the source of production.

The most vexing questions to the drug interests are presented by the vague and uncertain language of Sections 1006 and 1007, amending Sections 1 and 6 of the Act of Congress approved December 17, 1914, commonly known as the Harrison Act. These amendments well illustrate the viciousness of riders and the danger of permitting the extremist or over-zealous legislator to formulate radical amendments to existing laws. The attempt to strengthen the Harrison Act has resulted in increased confusion and difficulties to the Department as well as to the drug trade and medical practitioners. The re-licensing of those already licensed to act as manufacturers or distributors of opium, etc., until June 30, 1919, under an increased license fee, cannot be looked upon as necessary as a means of raising any additional revenue. The making of an additional inventory of the stocks on hand has been somewhat of a burden as well as a nuisance to these licensed distributors.

The attempt to classify the various dealers or distributors of the narcotics covered by the act by means of definitions has created some questions that will be exceedingly difficult for the Department to decide. The attempt has been to classify these as importers or manufacturers who shall pay $24 per annum, wholesale dealers $12, retail dealers $6, and medical practitioners who shall pay $3 per annum.

The definition for the first class named is "every person who imports, manufactures, compounds, or otherwise produces for sale or distribution any of the aforesaid drugs shall be deemed to be an importer, manufacturer or distributor." The bone of contention here is the meaning of the word "compounds" in the act. If the construction placed upon this be such as to cover the preparation of such medicines as paregoric, Bateman's drops or Brown mixture because opium in some form enter into these, then every person who manufactures such necessary pharmaceuticals becomes a compounder and subject to such tax as well as in any other class under which he may have to register.

The definition for a wholesale dealer is that "every person who sells or offers for sale any of said drugs in the original stamped

packages as hereinafter provided shall be deemed a wholesale dealer." Here again arises a serious question, as under the stamping provision every unit must be stamped and if the retailer sells on a prescription a tube of hypodermic or other tablets containing for example, morphine, in the original package or vial, which as a trade unit must be stamped, does he not become a wholesale dealer and subject to license as such?

The definition for a retail dealer is likewise somewhat involved as "every person who sells or dispenses from an original stamped package is deemed to be a retail dealer." As a physician must necessarily buy such articles as hypodermic tablets or other medicines containing any of these narcotics in stamped packages, does he not also become a retail dealer when he uses or dispenses same from these containers as under the law he must do? Will he have to be licensed under both classifications—physician and retail dealer?

The law provides that "there shall be collected a tax of one cent per ounce and any fraction of an ounce to be taxed as an ounce, the tax to be collected by an appropriate stamp affixed to the bottle or other container so as to securely seal the stopper, cover or wrapper thereto." Further that "it shall be unlawful for any person to purchase, sell, dispense or distribute any of these drugs except in the original stamped package, or from the original stamped package." The stamp is to be affixed by the importer, manufacturer, producer or compounder of the drug or preparation and so becomes a "manufacturers or 'producers' tax" and not a tax to be paid by a wholesaler or retailer on stock in hand.

A preliminary notice issued by some of the district collectors advising wholesale dealers, retail dealers, practitioners, etc., to affix these narcotic stamps to stock on hand was an error.

The wording of this section would appear to substantiate the opinion that this tax must be paid upon the ounce of the preparation, irrespective of the narcotic content.

The amended Section 6 of the Harrison Act permits the manufacturers and dealers in the articles exempted under the provisions of this section to register and procure narcotic supplies for such purpose by paying a tax of $1.00 per year; thus covering the manufacturers of this class of exempted articles who were not included with those licensed under the original Harrison Act. The retail drug trade, as well as other dealers, including dispensing physicians should note that the amended section now requires that a record

shall be kept of all sales, exchanges or giving away of such preparations and in such a manner as the Commissioner of Internal Revenue shall direct. Doubtless, in due time the form of this record will be prescribed. In the meantime such sales or dispensing should be recorded.

It is evident that in carrying out the tax stamp provisions that the same importation of opium, morphine, etc., may be repeatedly taxed as it passes through the hands of the importer and manufacturer before it finally reaches the dealer in the form of finished preparation, as in each subdivision of package or change of product, restamping will undoubtedly be insisted upon.

The difficulties of administering the law as it now stands and the innumerable questions which are bound to arise regarding the purport of the wording will probably necessitate further reconsideration and further amendment of the Harrison Act.

G. M. B.

TREASURY DECISION NO. 2788.

Under date of February 6, 1919, Commissioner of Internal Revenue D. S. Roper issued T. D. 2788 relating to Nonbeverage distilled spirits and wines, being "Instructions relative to the sale and use of distilled spirits and wines for other than beverage purposes under the food control act of August 10, 1917, and the acts of November 21, 1918, and October 3, 1917." As these have a direct bearing upon the necessary work of pharmacists they should be studied by them so that they may be complied with if at all practicable.

There are unfortunately a number of statements and departmental rulings in this promulgation that we are rompelled to criticise as contrary to the intent of the laws themselves and as unnecessary interferences with the legitimate practice of medicine and pharmacy.

The food conservation act of August 10, 1917, forbid the use of food materials in the production of distilled spirits *for beverage purposes* and provided that under such rules, regulations and bonds as the President may prescribe, such materials may be used for the production of distilled spirits exclusively *for other than beverage purposes.*

The act of November 21, 1918, reaffirmed this attitude of the government and provided: "The Commissioner of Internal Revenue

is hereby authorized and *directed to prescribe rules and regulations,* subject to the approval of the Secretary of the Treasury, in regard to the manufacture and sale of distilled spirits and removal of distilled spirits held in bond after June thirtieth, nineteen hundred and nineteen, until this act shall cease to operate, *for other than beverage purposes;* also in regard to the manufacture, sale, and *distribution of wine for sacramental, medicinal, or other than beverage uses.*"

The italicized portions as well as the context of these quotations, make it clear that the intent of Congress was that distilled spirits and wines were to be available for medicinal purposes. It would also appear that Congress recognized the need of distilled spirits and wines in their *pure state* as *medicines* and there is nothing whatever in the wording that would indicate that these must be "denatured" so as to render them unfit for medicinal use per se.

The present regulations while modifying prior decisions only reaffirm the attitude that the Department had assumed that pure alcohol and other distilled spirits and pure wines cannot be prescribed or dispensed for medicinal use. This decision would make the procuring of such after June 30, 1919, impossible and illegal even on prescription and the regulations evidence the purpose to interfere with the legitimate practice of medicine and pharmacy despite the intent of Congress as shown by the wording of the acts.

It is hard to reconcile the power to legislate vested by the Constitution solely in Congress, with the assumed authority of the executive departments to abridge or abrogate the laws or modify their evident intent. The Food and Drugs Act named the Pharmacopœia of the United States and the National Formulary as the authority for the standards of quality and purity for drugs and defines the meaning of the word drug. That definition and the standards fixed by the authorities named, remain the law of the Country until rescinded by Congress itself. The U. S. Pharmacopœia accurately defines and describes the legal standard for alcohol and under the existing law, only alcohol of the U. S. P. standard can be sold or dispensed when the drug alcohol is ordered. The Internal Revenue Department by an edict now sets aside this authorized and legal standard and decrees that even "on a physician's prescription" U. S. P. Alcohol "must not be dispensed" unless first denatured (adulterated within the meaning of the Food and Drugs Act) by the addition of a foreign poisonous substance and labelled "Poison." Under this decision, the law enacted as the

means of preventing adulteration of drugs, must be continuously violated by acts contrary to the judgment of the physician and to the detriment of his patient, and the evident intent of Congress in these enactments nullified.

The Department has not been entirely consistent in this decision. While denying to the patient suffering with fever the right to be rubbed down with pure non-beverage alcohol of the pharmacopœial standard, even though such medication is directed by the attending physician, the regulations nevertheless permit that "nonbeverage distilled spirits may be used for rubbing purposes in Turkish bath establishments," providing no charge is made for alcohol used in rubbing the customer. The proprietor of such an establishment easily complies with the regulations by making his service charge sufficient to include the value of the alcohol. Which of these is the use, deserving first consideration as coming within the designation "medicinal"? Which is the most necessary? and the most humanitarian?

The regulations provide that "spirits of a potable proof which were entered into warehouses and marked and branded as whisky, rum, gin, brandy, etc., will be presumed to be for use for beverage purposes when withdrawn or sold. Here again the "presumed" position will preclude the use of these as "medicinal" agents and annul the apparent intent of the law, although many of our most able physicians continue to consider these distilled spirits valuable as medicines.

From time immemorial, wines have been used as remedial agents as well as for solvents and preservatives of other medicinal substances. The regulations assert that "It is not *believed* that there is any legitimate use for wines for medicinal purposes, and since it is impracticable to determine the exact purpose of use when taken internally, except when used for sacramental purposes, no wines, as such, may be sold for internal use on a physician's prescription or otherwise as medicines." The "belief" of some official temporarily in a position of authority to render a decision is set up in opposition to the belief of thousands of capable physicians that wines are at times very necessary as medicines. It is not an uncommon experience that the administration of small portions of champagne wine, when the stomach will retain nothing else, has tided over the crisis and saved the patient's life. But under the existing conditions, ex-

perience and medical knowledge are not to be given credence or weighed against departmental "*belief.*"

Pharmacists and manufacturers may likewise have some difficulty to obtain the supplies of sherry or other wines needed for the manufacture of N.F. preparations and other standard formulas calling for wine as an ingredient. In the National Formulary we have upwards of a score of such formulas and the question confronting the Committee on N.F. and the pharmacists of the country is what changes may have to be made in these legal standards to comply with this irrational contravention and then a subsequent annoyance will be the explanations that may have to be made to customers and law officers of the deviations from the official formulas.

The homeopathic physicians are far from contented with the regulation "that a homeopathic physician or any other person may obtain from the pharmacist not exceeding 2 drachms of any attenuation, potency, or dilution at one time without filing bond or obtaining permit."

The question of solving the evil of intemperance can surely be attained by sane laws and regulations that will not interefere with legitimate medicinal practice and thereby imperil the lives of many of our people. Impractical and radical regulations may result in a reversion of public sentiment to such an extent as to actually defeat the purpose of the prohibitionists.

G. M. B.

PRIVATE—SECRET—PERSONAL—NO. 1.[1]

"Come, now, and let us reason together!"

By John Uri Lloyd, Phar.M.

In the opinion of this writer, misunderstanding of ideals and motives causes much of the trouble that prevails when, in anger, friend parts from friend. Neglect to define one's position properly and fully, on a problem that presents several viewpoints, may breed antagonisms where, could the two minds be brought together before prejudice was bred, harmony instead of discord would have resulted. Perhaps the misconception of the meaning of a word or words,

[1] Privilege of publication in a medical journal is extended the author.

where shades of distinction may perplex even an expert, holds men's minds apart. Comes first a one-sided impression, then, as discussion progresses, intensity of argumentative passion takes its place, next comes self-bred fanaticism in which the disputants forget the original cause, to make personal their grievances, which may finally lead to estrangement, even hatred, each of the other. Leaders may they now become of discordant factions, who jump at conclusions with not less vehemence than have their misled authorities. The perhaps obsolete meaning of a word may be the foundation on which one party stands,—the not less unimportant dictionary shading of that word's application may possess the other.

To meet together in friendly discussion of this or any other problem becomes now impossible,—individual hatred has made fanatics of one and all. Helpless to argument, as a fish in a net, is the man steeped in dogmatic fanaticism. Cast your eye about you, possibly the moté that rests therein may yet permit you to perceive the faults of others, who in turn see your mote as a mighty beam that obstructs your vision. To cast out these motes is as difficult as to take to one's self the time-honored text that heads this article,

"Come, now, and let us reason together!"

Many are the men deep-dyed in medical and pharmaceutical ethics, who during past decades delighted to bite and scratch and fight each other over the words "secret" and "private." To many men involved in the ethics of medicine, as well as pharmacy, these words were from every angle alike discrediting. And yet, in some directions, this writer believes that neither word, properly considered, is subject to criticism when applied to either legitimate pharmacy or ethical medicine. Indeed, he has been so bold as to assert, for many years, that the very leaders in self-made ethics laid down for others to follow, might well, before assailing a neighbor, search their own eye for the mote which perhaps needs, for location, neither microscope nor telescope.

Take your dictionary. Observe how liberal is the expert lexicographer concerning the shadings of this word SECRET: *"hidden; concealed; not revealed; private"* (Webster). Note that in establishing its authoritative use, appropriate quotations are offered, from various authorities: *"secret* graces and virtues are the hidden beauties of a soul." "A *secret* or silent prayer." Now contrast this

implied altruistic use of the word, with "I will have nothing *underhand.*" Between these rests a line of shadings that nearly parallel, in their contact meanings, the questionings of a fungus expert perplexed in his art. And yet, in the ethics of some authorities in medicine, but one thought applies to him who practices any phase of therapeutic *secrecy*. He is not of the Code,—altogether bad, he is "*irregular.*"

These years ago, this writer filled prescriptions for a talented physician, a regular of the regulars. In those days, oftener than now, the "*Code*" was used as an implement to distinguish between him outside the pale and him blessed by the code's all-wise protection. This physician stands yet in memory as a conscientious, gifted man, second to no other, professionally or ethically.

Consider now one of his patients, whose face rises to memory's call. Unconscious was she that, a hypochondriac, she was a representative of a peevish class. Medicine she *must* have, to live. To her, the (this) physician was next to the Infallible. And yet, time after time his prescriptions for her use were *bread pills,* dusted sometimes with cinnamon, again with licorice, and occasionally with wood ashes. Varied in size and color were they, to serve this lady's need, and well did they accomplish their purpose.

And yet, some there are who might argue that in comparison with deception such as this, quackery need not blush,—a problem each reader is entitled to settle to his own satisfaction. Another might assert that mind influence (cure) might justify its "cause" by this bread-pill example, a subject it is also unnecessary for us now to discuss.

Ask the physician of the olden time, whose patients would not take *calomel,* How many prescriptions of Hyd. Chlor. Mit. were written for these "fanatics." In those days, some persons believed that *quinine* "wracked the bones," and bred untold disorders. Cinchona, "the Jesuit's pernicious powder," was by some considered of the Devil's brew. Ask the physician of half a century ago how many prescriptions he wrote, for "Huxham's Tincture," where quinine would better have served their purpose?

In those days, it was the duty of the druggist to refrain from explaining to any layman the prescription's content. Is not this yet the proper rule? Did not this *secrecy* of the physician in his methods of prescription mysticism give rise to charges and innuendoes innumerable? Were not the very framers of the code against

secrecy in medicine, in the eyes of a great part of the public, the most pronounced of all secret practitioners? Did they not, in the opinion of many men, approach perilously near the "Black Art" in their use of cabalistic formulæ?

Do not accept that by citing these examples this writer makes an argument favoring the open door between physician and patient, in therapeutic agents. Instead, he believes that the physician should not be hampered by unqualified questioners. He should be implicitly trusted. He is called to treat our loved ones, because these patients cannot serve themselves. Never does this writer ask his physician the names of the remedies administered to a member of his family, or to himself.

The object of this phase of our discussion is to indicate that the term *secret* needs not, even with a physician, be always accepted in the sense some authorities might and do apply to it. The very province of the physician entitles him to the privilege of professional reserve that, for special service, even approaches deception, when the patient's welfare so demands. And, what of the pharmacist?

Knows anyone the pharmacist who to a physician's patient discloses the ingredients of a prescription? Instead, does he not ever sacrifice himself in financial directions to preserve inviolate the trust placed in him by the physician? Is he not constantly solicited to explain the prescription? Is not now, as fifty years ago, the answer: "Ask the doctor, I have no right to discuss the subject?" Does he not accept that *secrecy* as to some of the ingredients may be very necessary? Have we not examples of cases where the care of a physician as to overdoses was deplorably disturbed by patients who, getting the name of an ingredient, purchased the drug in bulk, to his distress? Behold we not today the evils of self-medication by him who purchases the fashionable synthetics that, in this writer's opinion, should be administered carefully, even by the physician who stands with his hand on the patient's pulse. Possibly greater *secrecy* might today be serviceable to humanity. Would it not be better had greater secrecy long since been practiced in some directions? Who knows the dire effects of some of the modern agents unwisely made familiar to the public? Well does this Nation comprehend the deplorable results of such as opium.

"Come, now, and let us reason together!" Concede that some forms of secrecy in therapeutics are closely akin to charlatanism, but that others may be necessary to the patient's comfort and welfare.

This leads us to a consideration of the word *private,* which is even more obnoxious to some persons involved in enforcing pharmacy ethics on their neighbors, than was the word *secret* to the "ethical purist" of the old-time medical code.

SOME OBSERVATIONS ON THE USE OF BORIC ACID AS A DISINFECTANT.[1]

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Two general procedures are available for the prevention of premature death, building up the body resistance and the destruction of infective agents in man's environment. Among the procedures which may be used to reduce the possibility of infection from environment, is disinfection. Many different chemicals and reagents are used to destroy pathogenic microörganisms some of which are of undoubted value while others, even though they may have rather extended application, may hardly be comprehended as having much destructive action toward bacteria. Among such a class of disinfectants we might expect to find boric acid. With some practitioners this is regarded as an efficient bactericide since they recommend its use at such occasions as child-birth and other occasions where it has been proven that the bacterial flora must be controlled.

Historical.

The literature is very extensive on the use of boric acid as a food preservative. Agulhon[2] found that boric acid solutions were not antiseptic. Bernstein[3] made a rather careful study of the use of this compound as a food preservative and secured some data which may be of interest in this connection. He reported a marked selective action on microörganisms inhibiting yeasts and members of

[1] From the Laboratories of Bacteriology of the University of Illinois, Urbana, Ill.

[2] Agulhon, Are Boric Acid Solutions Antiseptic, *Rev. mens. med. prat.,* 1912, 51.

[3] Bernstein, J., Preliminary Note on a New Aspect of the Effects of Boric Acid as a Food Preservative, *Brit. Med. Jour.,* No. 2572, 928–9.

the proteus group of bacteria. Members of the *B. coli* group were not affected. Strassburger[4] found the same selective action. This investigator states some organisms are able to stand large doses of boric acid with impunity while others find small doses very toxic. Agullion[5] found that this chemical in saturated solutions had little retarding effect on the activity of enzymes. E'we and Vanderkleed[6] have stated that two grains of boric acid would preserve a sample of urine for six days, whereas the control sample spoiled in three days. Kuehle[7] found that B_2O_3 was a very feeble antiseptic and in no way had the ability to check undesirable bacterial change. Such are the impressions which one is able to get from the literature concerning this subject.

Ochsner[8] stated that this chemical did not destroy pathogenic bacteria but did diminish their virulence.

Experimental.

No attempt was made to carry out an exhaustive investigation on boric acid as a disinfectant. An attempt was made, however, to determine just how toxic a solution of boric acid was toward bacteria. To do this, a saturated solution in distilled water was used. Chemical handbooks state that such a solution of this acid approaches a 4 per cent. solution. Such solutions are generally used in disinfection.

The first experiment consisted in adding increasing amounts of boric acid to melted dextrose agar and allowing the tubes to harden in the slanted position. After that the slants were inoculated by streaking and incubated. The incubation period was four days at 37° C. after which the culture tubes were observed. The results with common bacteria are given in Table I. The signs used therein have the following values: ++ = normal growth determined from an untreated agar culture; + = growth; — = no growth.

[4] Strassburger, F., Boric Acid as a Preservative with Reference to Its Use in the preserving of Crabs, *Hyg. Rund.*, 19, 169–85.

[5] Agullion, H., The Influence of Boric Acid on the Action of Diastasic Ferments, *Ann. Past. Inst.*, 29, 495–518. *Chem. Absts.*, 5, 1911, 1788.

[6] E'we, G. E., and Vanderkleed, C. E., Boric Acid as a Preservative for Urine Analysis, *J. Amer. Pharm. Assoc.*, 2, 979–982.

[7] Kuehle, H., Boric Acid as a Preservative, *Pharm. Centr.*, 50, 559.

[8] Ochsner, E. H., The Biochemistry of Topical Applications with Special Reference to the Use of Boric Acid in Septic Infections, *Chemical Abstracts*, 12, 1918, 191.

An examination of this table seems to indicate very little if any germicidal action of the boric acid even when added to the agar in rather large amounts. *P. fluorescens liquefaciens* seemed to be

TABLE I.

Organism.	Number of Cubic Centimeters of Saturated Solution Boric Acid Added to Each Tube of Agar.									
	.1.	.2.	.3.	.4.	.5.	.6.	.7.	.8.	.9.	1 cc.
B. arborescens	−	−	−	−	−	−	−	−	−	−
B. aërogenes	++	++	+	+	+	+	+	+	−	−
B. capsulatus	++	++	+	+	+	+	+	+	+	±
B. cereus	±	±	−	−	−	−	−	−	−	−
B. cloacæ	++	++	+	+	+	+	+	±	±	±
B. colon	++	++	++	++	+	+	+	+	+	+
B. cyanogenus	++	+	+	+	−	−	−	−	−	−
B. dysenteriæ	+	+	+	+	+	−	−	−	−	−
B. enteritidis (Gaertner)	++	++	++	+	+	+	+	+	+	+
B. fluorescens liquefaciens	+	+	+	−	−	−	−	−	−	−
B. gasoformans	++	++	++	++	+	+	+	+	+	−
B. granulosum	+	+	+	−	−	−	−	−	−	−
B. of hog cholera	++	++	++	++	++	+	−	−	−	−
B. mesentericus	++	++	++	+	+	−	−	−	−	−
B. proteus vulgaris	++	++	++	++	++	+	−	−	−	−
Strep. byogenes	++	++	++	++	++	+	+	+	+	+
B. paratyphosus "A"	++	++	+	++	+	±	±	±	±	−
B. paratyphosus "B"	++	++	+	+	+	+	−	−	−	−
B. typhosus	++	+	+	+	+	+	+	+	±	±
B. pyocyaneus	++	++	++	+	+	+	−	−	−	−

affected to the greater extent since it did not grow on agar slants with over 0.4 Cc. of saturated boric acid solution. A few other organisms as indicated in the table seemed to be inhibited when quantities of saturated boric acid solution approaching 1 Cc. were used. It is possible that a selective action may be secured when this reagent is added to agar.

In order to use a different environment and a fluid medium, the same experiment was repeated with Frankel's solution which had the following composition: 5 Gms. sodium chloride, 2 Gms. monocalcium phosphate, 6 Cc. ammonium lactate, 4 Gms. asparagin, 1 liter distilled water, 20 Cc. *N* sodium hydroxide. To 5 Cc. of this solution were added increasing quantities of saturated boric acid solution after which the tubes were inoculated with pure cutlures and incubated at 37° C., using in each case the same amount of inoculum. The results are shown in Table II.

From this table it is apparent that any inhibitory power possessed by boric acid is not constant. Little decrease in growth was

TABLE II.

Results—Organism.	Number of Cubic Centimeters of Saturated Solution of Boric Acid Added to 5 Cc. of Frankel's Solution.									
	.1.	.2.	.3.	.4.	.5.	.6.	.7.	.8.	.9.	1 Cc.
B. arborescens	+	+	+	−	−	−	−	−	−	−
B. capsulatus	++	++	++	++	++	++	+	+	−	−
B. cereus	++	++	++	+	+	+	−	−	−	−
B. claocæ	++	++	++	+	+	+	+	+	+	+
B. colon	++	++	++	++	+	+	+	+	+	+
B. dysenteriæ	++	++	++	++	+	+	+	−	−	−
H. enteritidis	++	++	+	+	+	+	+	+	+	+
B. fluorescens liquefaciens	++	+	+	+	+	+	+	−	−	−
B. gasoformans	++	++	+	+	+	+	+	+	+	+
B. granulosum	++	++	++	++	++	+	+	+	+	+
B. of hog cholera	++	++	+	+	+	−	−	−	−	−
B. mesentericus	++	++	++	++	+	+	+	−	−	−
B. proteus vulgaris	++	++	++	++	+	+	−	−	−	−
P. pyocyaneus	++	++	++	++	++	++	+	+	−	−
Strep. pyogenes	+	+	+	+	+	+	+	+	+	+
B. paratyphosus "A"	++	++	+	+	−	−	−	−	−	−
B. paratyphosus "B"	++	++	++	+	+	+	+	−	−	−
B. typhosus	++	++	+	+	+	−	−	−	−	−

secured until after 0.6 Cc. of the acid were added to 5 Cc. of Frankel's solution.

In order to use a larger amount of the boric acid, the silk thread method, which has been so serviceable in the past in similar studies, was used.

Sterile white silk threads one inch long were placed in broth suspension of the organism for 1½ hours. They were then re-

TABLE III.

Results—Organism.	Time in Minutes that a Silk Thread Impregnated with the Organism was Exposed to Saturated Boric Acid.									
	5.	10.	15.	20.	25.	30.	35.	40.	45.	50.
B. arborescens	++	++	++	++	++	++	++	++	++	++
B. coli	++	++	++	++	++	++	++	++	++	+
B. enteritidis	++	++	++	++	++	++	++	++	++	++
B. typhosus	++	++	++	++	++	++	−	−	−	−
B. paratyphosus "B"	++	++	++	++	++	++	++	++	++	++
B. cereus	++	++	++	++	++	++	++	++	++	++
B. capsulatus	+			+						±
B. cyanogens	++	++	++	++	++	++	++	++	++	+
B. proteus vulgaris	++	++	++	++	++	++	++	++	++	++

++ normal. + some growth. — no growth.

moved with a sterile platinum needle, placed into sterile Petri dishes and placed in 37° C. temperature room over night (ten

threads to each organism). Each thread was then placed in a saturated solution of boric acid and exposed, respectively, 5, 10, 15, 20, 25, 30, 35, 40, 45 and 50 minutes, after which each thread was placed in a tube of sterile plain broth and incubated at 37° C. for one week.

Controls were made for each organism by placing the dried thread (from the suspension) directly without exposure to boric acid, into tubes of plain broth.

A check was also made on the boric acid by placing one Cc. boric acid in a tube of plain broth and incubating at 37° C. The results of this experiment are shown in Table III.

Even under these conditions, boric acid exhibited very little inhibitive effect on bacteria. In this experiment the entire saturated solution was available for action toward the bacteria. A saturated solution of the boric acid when allowed to act on the organisms for 50 minutes did not kill them. Bacillus typhosus was killed by 35 minutes' exposure to the saturated boric acid.

An attempt was made to determine whether boric acid, acting as an antiseptic, would effect yeast fermentations. It seemed to possess no consistent action since in many cases more gas was formed after exposure to boric acid than before. Under the conditions of this experiment the boric acid seemed to have no antiseptic activity in reducing the zymogenic activity of the yeast.

Conclusions.—A prominent writer on preventive medicine has stated that boric acid was a "camouflage" disinfectant. Such seems to be the result of this short study. The use of this reagent in those cases where disinfection is absolutely essential, should be discontinued. It seems probable that many of the salts of boric acid may have as limited a disinfecting power as the acid itself. The statements of the vendors are possibly misleading.

DIGITALIS PURPUREA.

By George P. Koch, Ph.D., and J. Russell Butler.[1]

Introduction.

The cultivation of digitalis in the United States, as in the case of belladonna and hyoscyamus, has resulted to a great extent from the European war. Since our principal source of supply was cut off, there naturally resulted a great advance in the price paid for digitalis leaves. Harvesting the large amount of digitalis which grew wild in the western part of Washington and Oregon and other states did not overstock the market. A considerable number of individuals attempted to grow digitalis on a commercial scale, but, due to inexperience with such a crop, there results the first few years were more or less failures. At present, however, growing digitalis has passed the experimental stage and a successful crop can be grown on a commercial scale. In those localities where these plants grow very luxuriantly under uncultivated (wild) conditions, it would require a comparatively small amount of attention to grow it commercially. To study digitalis so that a successful and paying crop can always be obtained in localities which are not so favorable for its growth, a number of experiments were made covering the most important phases of cultivation of this plant.

Study of the Germination of Digitalis.

Viable digitalis seeds, as seeds of other medicinal plants, have been difficult to procure. This is principally due to the fact that in those localities of the United States where digitalis has been cultivated for commercial purposes, the winters are so severe that if the plant is to be grown as a biennial or perennial, the roots have to be removed from the soil in the late fall and stored under cover. This is a rather expensive undertaking, and has discouraged the growing of digitalis as a perennial plant.

The seeds of digitalis are very small and usually not very viable. Stockberger (14) states that they do not germinate very well except when under the very best cultural conditions. Newcomb (11) finds

[1] The authors are indebted to Dr. Paul S. Pittenger for having made the alkaloid determinations and take this opportunity to express their thanks in this connection.

that it requires from 9 to 15 days for digitalis to germinate. Borneman (5) states that digitalis plants come through the ground in about 9 days and at the end of three weeks, will be ready for transplanting into pots or in plats.

To determine whether or not the blotting paper method of germinating seeds could be applied to testing the viability of digitalis and at the same time, to determine how long a period of time it requires for seed of digitalis to germinate, two samples of 100 seeds each were germinated between blotters.

TABLE I.

SHOWING THE LENGTH OF TIME IT REQUIRES DIGITALIS SEED TO GERMINATE BETWEEN BLOTTING PAPER.

Sampl No.	Percentage of Seeds Germinated.			
	4th Day.	5th Day.	7th Day.	9th Day.
1	76	78	84	87
2	76	79	84	86

With the above sample of digitalis seed, 86 per cent. germinated on the ninth day. It will be seen that very few more had germinated on the ninth day than on the seventh. This method of testing the viability of digitalis seed proved very successful. By applying it to four other samples of digitalis seed, it was found that these tested 91, 87, 42 and 7.5 per cent. It is apparent from these figures that there is a great variation in the viability of digitalis seed.

Digitalis seed planted on the soil were covered with a small layer of sand. Those were kept moist and to prevent excessive evaporation were covered with burlap. Most of the sprouts were out of the soil and were ¾ inch high on the sixth day after planting.

STUDY OF THE PLANTING OF DIGITALIS.

What is the most satisfactory method of planting digitalis? Stockberger (14) says, "Sowing the seed directly in the field occasionally gives good results, but is so often unsuccessful that it can not be recommended." Miller (10) germinated digitalis seed in the greenhouse the first week in December, grew the plants in flats until the middle of March, after which time he put them in a cold frame until May when they were planted in the field. Borneman (5) says that digitalis plants come through the ground in about

nine days. Three weeks after this period, they will be ready to transplant into pots or in flats. He states further, that after they have attained the height of about 6 inches, they will be ready for planting in the permanent bed. He recommends planting the plants 24 inches apart in the rows, and the rows three feet apart. Newcomb (11) after germinating the seeds, transplanted the plantlet in flats. They were grown until they were large enough to transplant into 2 to 2½ inch pots. Later, they were planted in the field.

With the high cost of labor in the United States, it is very evident that commercially, by employing the above method, we could not be very successful, unless a high price was received for dry digitalis leaves. To reduce the cost of production as much as possible, an idea of growing the plants directly in small pots was tried. One hundred 1¾ inch pots were filled with a light compact soil and then seeded with digitalis seeds. The seeds were covered with a light layer of sand. The pots were kept moist by watering carefully twice a day and to prevent excessive evaporation, were covered with burlap until the seed had germinated. The seed was sown on May 10, and on June 13 the plants were in fine condition. As there were from 6 to 15 plants in each pot, they were thinned out so that but 3 or 4 remained in each pot. This was a very easy task and required but little time as the whole mass of plants and soil were removed from the pot and this was divided into from 2 to 4 parts, depending upon the number of plants present. Two weeks after thinning out, the plants were large enough to plant in the field. At this period, they were about 2 inches high and planting the soil from the pot with the roots, left the roots intact and the plants grew at once when transplanted in the field. Hence, it will be seen that by the above method, three steps were required until the digitalis plants were finally in the field. This method having proved successful, it, with a few modifications, was employed in growing the commercial material. If a planter, such as a tobacco planter, is employed in transplanting the plants in the field, it is desirable to have the plants slightly larger than 2 inches. In 4 to 6 weeks after thinning out, such plants could be obtained.

Is it possible to secure a satisfactory crop by seeding digitalis seeds in the field directly? Experiments were made covering this factor. It was found that ordinarily the weed seeds germinated so readily that the digitalis plantlets were hard to find among the weeds. Were it possible to keep the plant beds entirely free from

weeds, seeding directly in the field would be a satisfactory method of procuring the plants.

Effect of Fertilization upon the Growth of Digitalis.

Formerly there was considerable discussion concerning the relative alkaloidal activity of the wild and garden grown leaves of digitalis. Several investigators were of the opinion that digitalis grown wild in its natural habitat, had a higher activity than that which was cultivated. On this phase, Hall (6) concludes that there is not necessarily any difference in the activity of wild and garden grown digitalis. In determining the effect of various inorganic fertilizers upon digitalis, Miller (10) found no appreciable differance in the activity in plants which received fertilizers, and in the controls. With regard to digitalis seed bed, Borneman (5) states that the soil for seeding should be well prepared, having been limed and well mulched. Holm (7) says that fox gloves grew best in well drained loose soil, which is mixed with leaf mold, but it does not grow in calcareous soil.

TABLE II.

Showing the Effect of Inorganic Fertilizers upon the Growth of Digitalis in a Clay Loam Soil.

Fertilizer Application [3]	Wt. of Plants, Grs.	Average, Grs.
1. No fertilizer	7.0	
2. No fertilizer	8.5	7.7
3. Complete fertilizer	11.0	
4. Complete fertilizer	10.7	10.8
5. Complete fertilizer—$Ca(H_2PO_4)_2H_2O$	9.3	
6. Complete fertilizer—$Ca(H_2PO_4)_2H_2O$	10.3	9.8
7. Complete fertilizer—K_2SO_4	9.0	
8. Complete fertilizer—K_2SO_4	10.0	9.5
9. Complete fertilizer—$NaNO_3$	8.2	
10. Complete fertilizer—$NaNO_3$	8.5	8.3
11. Complete fertilizer—$CaCO_3$	10.0	
12. Complete fertilizer—$CaCO_3$	8.0	9.0

An experiment testing the effect of various fertilizers upon the growth and development of digitalis in soil was determined. Ordinary 5-inch flower pots were filled with 1,000 Gm. of a clay loam soil, taken from the premises of the Mulford Biological Labora-

[3] Complete fertilizer—1,000 lbs. $CaCO_3$, 800 lbs. $Ca(H_2PO_4)_2H_2O$, 400 lbs. K_2SO_4, 600 lbs. $NaNO_3$ and 100 lbs. $MgSO_4$ per acre of 2,000,000 lbs.

tories. Fertilizers were applied as shown in the table below. Seeds were planted on May 28, and about 6 months later, the plants were harvested and dried in the oven at 100° C. for 4 days. The moisture conditions were maintained at the physical optimum of the soil.

On studying the results of Table II, it will be seen that adding fertilizers to this heavy clay loam soil increased the growth of digitalis to some extent, however, in most of the cases, the increase was comparatively small. In the determination where a complete fertilizer was applied, the increase in weight over the control was greatest. In the pots where no sodium nitrate was added, the weights of digitalis harvested was very little more than in the control which recevied no fertilizer.

To more fully determine the absolute fertilizer requirements of digitalis plants, the above recorded fertilizer experiment was repeated using sand. The results of this experiment are presented in Table III.

TABLE III.

SHOWING THE EFFECT OF INORGANIC FERTILIZERS UPON DIGITALIS PLANTS IN SAND.

Lab. No.	Fertilizer Application.	Weight of Plants, Grs.	Average, Grs.
421	No fertilizer	1.7	
422	" "	1.3	1.4
423	" "	1.1	
424	Complete fertilizer[4]	4.7	
425	" "	2.3	3.1
426	" "	2.4	
427	Complete fertilizer—$Ca(H_2PO_4)_2H_2O$.	1.5	
428	" " "	1.9	1.5
429	" " "	1.2	
430	Complete fertilizer—K_2SO_4	3.9	
431	" " "	3.7	3.7
432	" " "	3.5	
433	Complete fertilizer—$NaNO_3$	2.2	
434	" " "	2.5	2.3
435	" " "	2.3	
436	Complete fertilizer—$CaCO_3$	3.5	
437	" " "	2.3	3.2
438	" " "	3.8	

It is very apparent from the results shown in Table III that certain inorganic fertilizers were necessary for the maximum growth

[4] Complete fertilizer—1,000 lbs. $CaCO_3$, 800 lbs. $Ca(H_2PO_4)_2H_2O$, 400 lbs. K_2SO_4, 600 lbs $NaNO_3$ and 100 lbs. $MgSO_4$ per acre of 2,000,000 lbs.

of digitalis. Phosphorus and nitrogen seemed to be the elements which the digitalis plants needed most. In the determinations where no phosphorus was supplied, the growth of digitalis was about the same as the controls. This would indicate that the other fertilizers supplied were not effective in increasing the plant growth until some available phosphorus was furnished. There seemed to be sufficient potash and lime in this sand to fulfill the needs of digtalis, as the growth of digitalis in the determinations where these were absent: 430, 431, 432 and 436, 437, 438, respectively, was as large as that in the determination receiving a complete fertilizer.

Effect of Certain Inorganic Salts upon the Growth and Alkaloid Content of Digitalis.

Certain inorganic salts stimulate the growth of some agricultural plants. Salts of manganese have this property. Boname (4) and others have shown that manganese in small amounts occurs in various soils and plants. Rogers and Newcomb (13) state that manganese appears to be a constant constituent of digitalis leaves, but the amount varies with the source from which the samples are obtained. Alpers (2) states that digitalis is generally found growing in soil which contains iron and manganese. It is true that all soils contain a certain amount of iron and according to Boname (4), soils contain a certain amount of MnO_2. According to Gehe (2), it is due to the lack of these elements (Mn and Fe) that digitalis does not occur in Switzerland.

To determine if salts of manganese or iron affected either the growth or the alkaloid content of digitalis when grown in soil, a pot experiment was carried out under controlled conditions. Into each of fifteen 5 inch pots, 1,000 Gm. of a clay loam soil (the same as used in the above pot experiment) were weighed. The same amount of a complete fertilizer of 800 lbs. $Ca(H_2PO_4)_2 2H_2O$, 400 lbs. K_2SO_4, 600 lbs. $NaNO_3$, 1,000 lbs. $CaCO_3$ and 100 lbs. $MgSO_4$ per acre of 2,000,000 lbs., was added to each pot. To six pots, manganese sulphate ($MnSO_4$, $5H_2O$) in amounts usually applied in field experiments with agricultural crops, was added; to six others, ferrous sulphate ($FeSO_4$, $3H_2O$), and the other three determinations were used as controls receiving neither salts of Mn or Fe. Digitalis seed was planted in these pots on May 28, and after the plants were about 2 inches high, they were thinned out to an equal number in

each pot and harvested after six months. The moisture was maintained at the physical optimum of the soil. After harvesting, the digitalis leaves were dried and the alkaloid determinations made.

TABLE IV.

SHOWING THE EFFECT OF MANGANESE SULPHATE AND FERROUS SULPHATE, APPLIED TO A CLAY LOAM SOIL, UPON THE GROWTH AND ACTIVITY OF DIGITALIS.

Pot No.	Treatment Lbs. per Acre of 2,000,000 Lbs.	Weight of Dry Material in Gms.	Average Weight in Gms.	Activity. Per Cent.
701	No treatment	6.5		
702	" "	5.0	6.1	83
703	" "	6.7		
704	75 lbs. $MnSO_45H_2O$.....	7.0		
705	" " "	8.0	7.0	76
706	" " "	5.9		
707	150 " "	7.2		
708	" " "	6.5	6.6	100
709	" " "	6.2		
710	75 " $FeSO_43H_2O$	7.7		
711	" " "	6.2	6.5	90
712	" " "	5.7		
713	150 " "	6.5		
714	" " "	6.0	6.1	90
715	" " "			

The results of the experiment above show that neither application of manganese or iron sulphate were effective in increasing the yield of digitalis in this soil, as the results are all within experimental error. From this, we would conclude that this soil either was sufficiently supplied with manganese and iron for the needs of digitalis, that the absorptive and adsorptive effects of this soil were so great that such amounts as were supplied were taken from the field of activity when they could be utilized by the plant, or that these salts were not essential for digitalis. There was a considerable variation in the activity of the samples of digitalis harvested from the pots which received the various treatments of the salts. This difference in activity is most marked between the samples receiving no treatment and those using 150 lbs. $MnSO_45H_2O$. Applying this amount of $MnSO_45H_2O$ was effective in increasing the activity 17 per cent. over that of the control. In the case of the determination receiving iron, there is an indication of increase in activity but this may be almost within experimental error.

Insects and Diseases Affecting Digitalis.

Digitalis plants, quite different from hyoscyamus and belladonna, Koch (8), (9), are not attacked by the various chewing and sucking insects. Hence, they require no spraying nor such particular attention as hyoscyamus and belladonna. It was noted that grasshoppers will chew the leaves, but as yet, the destruction by grasshoppers has been negligible.

A fungus disease, having all the characteristics of root rot, was found present on several digitalis plants in the field. This did not prove very destructive, as only a few plants were attacked and in these cases, the plants withstood the attack of this fungus.

Effect of Drying at Different Temperatures upon the Activity of Digitalis.

Opinions with regard to the methods of drying digitalis leaves, seem to differ considerably. Alpers (1) says the leaves should be dried at once as completely as possible, in a well ventilated drying closet at a temperature not exceeding 100° C. Perrot and Goris (3) propose the method of sterilizing the leaves, thus destroying the enzymes, when first drying digitalis leaves.

Borneman (5) concludes that the digitalis plants should be dried quickly by artificial heat, the temperature being brought up to 100° C. as soon as possible and maintained at this point.

Newcomb (12) summarizes in drying digitalis, applying artificial heat in a closet at a temperature of 75 to 100° C. for 8–10 hours a day, required 3 days to reduce the moisture to 4 per cent. By this method, the green color was never lost. He says that these methods were particularly suitable in that the leaves were quickly dried, it fixed the desirable green color, and at the same time, the active principles were not in any way injured.

An experiment on determining the effect of drying under various conditions on the activity of digitalis leaves, was made. A large sample of about 6 kilos of digitalis leaves was cut into small portions. After thoroughly mixing this material, it was divided into five samples of equal size. Each of these samples were dried at a different temperature, as shown in the table below. After drying these samples, they were submitted for analysis.

TABLE V.

SHOWING THE ACTIVITY OF DIGITALIS LEAVES DRIED AT VARIOUS TEMPERATURES.

Sample No.	Conditions of Drying.	Activity Per Cent.
1.	Out of door temperature 28° C.	166
2.	In oven 55–60° C.	142
3.	In oven 100° C.	166
4.	Heated in oven at 100° C. 1 hr. then dried at 55–60° C.	166
5.	Heated in autoclave 15 lbs. pressure for 1 hr. then dried at 55–60° C.	125

That the conditions of temperature under which digitalis leaves are dried influence their activity is quite apparent. The samples dried in the oven at 100° C., and heated in the oven at 100° C. for an hour then dried at 55–60° C. had the same activity as that which was dried spontaneously at a temperature of 28° C. On comparing the results of the three above mentioned with the results of the sample dried at 55–60° C., it is seen that 55–60° C. is an undesirable temperature, if the highest activity is to be secured. The explanation for the low results of the sample dried at 55–60° C. as compared with that dried at 100° C., is that in the former case, the activity might have been lost due to enzyme action as has been stated by investigators, previously referred to, while in the latter case, the enzyme activity was stopped at once. Autoclaving at 15 pounds pressure for one hour then drying at 55 to 60° C. proved too destructive, as the results of samples treated by this method were 41 per cent. less in activity than the sample which was heated in the oven at 100° C. and then dried at 55 to 60° C.

SUMMARY.

From the results of the experiments with digitalis, we summarize as follows:

1. The ordinary blotting paper method proved satisfactory for determining the viability of digitalis seeds.

2. By the blotting paper method, using good viable seed, 86 per cent. germinated in 9 days.

3. The viability of digitalis seed was variable, being from 7.5 to 91 per cent. viable.

4. When planting digitalis seeds in soil, most of the seeds had sprouted and were ¾ of an inch high on the 6th day after planting.

5. The most economical method of securing digitalis plants in the greenhouse, is to sow the seed directly in small pots. After

they have reached the height of 2 inches, thinning them out to from 3 to 5 plants per pot and then letting them grow several weeks longer before planting in the field.

6. From the practical standpoint, seeding digitalis directly in the field proved unsuccessful.

7. Inorganic fertilizers applied to a clay loam soil were effective in increasing the yield of digitalis. A complete fertilizer of 1,000 lbs. $CaCO_3$, 800 lbs. $Ca(H_2PO_4)_2H_2O$, 400 lbs. K_2SO_4, 600 lbs. $NaNO_3$ and 100 lbs. $MgSO_4$ per acre of 2,000,000 lbs., gave the best results. With this soil, sodium nitrate seemed to be the most essential single fertilizer.

8. In sand, calcium phosphate (monobasic) was the most important single fertilizer necessary for digitalis.

9. Neither manganese sulphate nor ferrous sulphate, applied in amounts of 75 or 150 lbs. per acre of 2,000,000 lbs. of a clay loam soil, encouraged a larger growth of digitalis. One hundred and fifty pounds per acre of manganese sulphate applied to a clay loam soil, increased the activity of digitalis 17 per cent. over the activity produced in plants grown in soil receiving no manganese sulphate.

10. Chewing or sucking insects do not seem to attack digitalis plants. A fungus disease, which has all the characteristics of a root rot, attacks digitalis plants, but has not been found to be very destructive.

11. Drying digitalis leaves at 100° C., or heating for one hour at 100° C. and then drying at 55–60° C., were the most satisfactory methods from the standpoint of both the amount of activity, as well as from the speed with which the drying is accomplished.

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THE PHARMACEUTICAL CHEMIST AND THE SCOPE OF HIS WORK.[1]

BY FRANK O. TAYLOR.

Each of us is prone to magnify the importance of that particular branch of chemistry in which he is actively engaged, so perhaps I may be pardoned for what, to many of you, may seem a biased and erroneous opinion, or evidence of a dense ignorance concerning other fields of chemical endeavor, when I say that I believe no field of chemistry is of greater scope or more varied character than that of pharmaceutical chemistry. And yet, I hope to give you such reasons for the faith that is in me that, if not fully agreeing, you

[1] Address before the Detroit Section of the American Chemical Society, January 16, 1919. Reprinted from *The Journal of Industrial and Engineering Chemistry*, March, 1919.

may at least recognize a measure of justice in this claim and have a better understanding of the reasons back of it.

Pharmacy has to do with the compounding and dispensing of medicinal products and is most frequently thought of in the very narrow sense of mere mixing together of various individual substances, or the extraction of drugs with the proper solvents and dispensing in suitable form for use, the whole process involving only a very moderate degree of chemical knowledge.

It is to this extremely limited scope that the term "pharmaceutical chemistry" is all too frequently confined. I wish to direct your attention, however, to pharmaceutical chemistry in its broadest sense as being the chemistry of medicinal substances, pertaining to their origin, preparation, dispensing, and effects, and the remarkable and varied ramifications of these subdivisions. Far from being a limited and somewhat isolated division of chemical science there is, I believe, no other branch of chemistry that needs for the solution of its diverse problems so many otherwise distantly related portions of chemical knowledge.

The metallurgist, who from the iron ore of northern Michigan produces by reactions in blast furnace and Bessemer converter, iron and steel of varied composition; or from the scarlet cinnabar of southern California wins the mercury for use in physical instruments and amalgams; or from the ores of Missouri obtains in giant smelters the zinc for innumerable industrial uses, may often forget that iron is intimately associated with vital processes, as in the red blood corpuscles, and plays an important rôle as a curative agent; that the mercury salts are used in combating some of the most deadly and insidious diseases, or as highly effective germicides and antiseptics; that the zinc in one form may be intensely escharotic and in another may be the basis of mild and healing ointments of wide use.

The agricultural chemist, who makes two blades of grass or ears of wheat grow where only one grew before, may also develop digitalis or belladonna or hydrastis or cannabis in greater abundance or of higher potency.

The glass chemist may have his skill taxed to produce ampoules of glass free from excess alkali and easily workable in a blow-pipe flame or free from soluble iron salts that rapidly decompose such substances as hydrogen peroxide or adrenalin.

The coal-tar industry contributes from its cruder products the

so-called "dead oils" as a basis for disinfectants of considerable potency; pure cresylic acids, to make antiseptics for surgical or general use; and phenol for use as such or in various compounds such as phenyl salicylate (salol) or the phenolsulphonates of zinc and calcium.

The dye chemist furnishes for medicinal use such things as phenolphthalein, so widely employed as a laxative; phenolsulphonaphthalein as a test for activity of the kidneys; scarlet-red for stimulating healthy and rapid growth of skin over surfaces denuded by burns or other accidents; acriflavine, but recently recommended in solution as a surgical dressing for extensive wounds, to be used in a manner similar to the sodium hypochlorite solution, known as Dakin's Solution, being destructive to bacteria in high dilution and apparently harmless to living tissues; malachite green proposed and widely experimented with for the same purposes; or methylene blue, so extensively used in certain types of urethritis.

Physical chemistry lends its aid in the production of such remedial agents as colloidal solutions of silver, mercury, sulphur, etc., obtained either by direct electrolytic action or in the presence of proteins, and adds to our slowly acquired empirical knowledge of emulsions an understanding of the reasons why, and the conditions under which the best results may be obtained.

Radiochemistry finds its pharmaceutical application in the use of ultra-violet rays for sterilizing water or various solutions, or the employment of radium salts and radioactive solutions in the treatment of various diseases, notably cancer.

The petroleum industry gives to the pharmaceutical chemist solid and liquid petrolatum of varying degrees of purity ranging from cruder petrolatum for veterinary ointments to the most highly purified liquid oil intended for human use as an intestinal lubricant, and paraffin as an ingredient of ointments or base of surgical dressings for application to extensive superficial wounds or burns.

The consideration of oils and fats, both vegetable and animal, applied one way or another to medicinal use, opens up another wide range through which our chemical investigations may lead us, including such things as the familiar castor and cod-liver oils; the intensely active cathartic, croton oil; that relic of old-time pharmacy, citrine ointment, made from lard, nitric acid, and mercury by a process similar to the familar elaidin test for olive oil; the comparatively little known chaulmoogra oil, which has been used with

some measure of success in the treatment of leprosy in India and our own southern states, and was some years ago the subject of extensive chemical investigation; oil of chenopodium or American wormseed, used first as an ordinary anthelmintic and more recently as a highly successful agent in destroying the hookworm, the bane of existence to so many thousands of people in warmer climates; and a great array of other fixed and volatile oils. And these things suggest at once a multitude of gums and resins of more or less interest medicinally, but which we will pass by.

In that limitless domain to which we refer in general as "organic chemistry," including therein those things particularly connected with physiological and biological chemistry, there exists a tremendous number of substances of great interest to the pharmaceutical chemist and there lie before him untouched fields for investigation that almost stagger the imagination. In this category appear substances of natural origin and of synthetic production—the alkaloids of aconite, opium, belladonna, stramonium, ergot, nux vomica; the comparatively innocuous glucosides of cascara or the highly toxic ones from strophanthus and digitalis; the digestive ferments such as pepsin, diastase, pancreatin; the endocrine glands and their derivatives, such as the suprarenal whence comes adrenalin, so marvelously potent in its effects on the blood pressure that one-twentieth of a milligram will show pronounced effects on a man; the thyroid, from which but recently an active iodine-bearing substance has been isolated; the pituitary gland of inestimable value in obstetrical practice and in the treatment of surgical shock; and others still less understood. Then we have that formidable and continually increasing array of synthetic substances, some of which, like acetylsalicylic acid (aspirin), or acetphenetidin (phanacetin), are part of the equipment of almost every household medicine cabinet, and others that you and I never heard of and probably never will.

These brief citations give some idea of the infinite variety of work presented to the chemist who deals with medicinal products but do not give any adequate conception of the great number of unsolved and abstruse problems which still lie before us and to which I will refer presently. You can at least see that the chemical knowledge of the man who has to do with pharmaceutical problems in their fullness must be extensive and that he will certainly have no monotonous existence.

Specific examples of some of the interesting questions that arise, which in some instances are very easy of solution and in other cases give us problems that promise to remain unsolved for an indefinite time in the future, will serve to give a more concrete conception of the requirements of the man who has to do with the development and production of medicinal substances in their widest scope.

Remember also that sometimes the solution of the simplest problems may involve the saving of hundreds or even thousands of dollars to the manufacturer who is producing medicinal substances on a very large scale. A question that may be of no particular moment when the quantity involved is only a few ounces becomes of intensest interest when it may mean the difference between entire loss or the satisfactory distribution of hundreds of pounds or thousands of pints of medicinal compounds of properly high quality.

Take so simple a thing as the almost universally used mild tonic, Beef, Iron, and Wine. Why should continual trouble be experienced with the development of pressure in the bottles, the evolution apparently of carbon dioxide, and continual breaking of packages and consequent loss? "Fermentation, of course," will be your first answer, and the fact that carbon dioxide is evolved seems excellent evidence that this supposition is correct, but fermentation is not likely to occur in a product that contains 18 per cent. alcohol, and furthermore, this explanation is impossible when the trouble continues after the product has been thoroughly sterilized in an autoclave and proven sterile by bacteriological tests. The solution when found is very simple and is that due to the action of the actinic rays of light the ferric citrate in the slightly acid solution is reduced to a ferrous salt with liberation of carbon dioxide. If a ferrous salt is originally used, there is no such trouble, and if the ferric salt is employed, the product must be carefully protected from bright light, especially direct sunlight.

Take another case: Why should breakage in ampoules containing cacodylates be very much greater than with any other of the solutions usually prepared in this form? There was no pressure developed and no decomposition of the solutions could be detected. The fact that the breakage occurred largely at the extreme end of the capillary tip, where the ampoule is finally sealed in a blowpipe flame, gave a clue, and the solution of the problem was that traces of the cacodylate solution adhering to the glass were decomposed just at the tip where the flame is used for sealing; the arsenic com-

bined with the glass, forming a ring of arsenical glass, which is entirely different in coefficient of expansion from the remainder of the ampoule and very brittle, hence comparatively slight changes in temperature frequently caused the tip to snap off. On putting into effect means for carefully washing out the tip of the ampoule with distilled water before sealing, the trouble disappeared.

Again, in the manufacture of antiseptic tablets containing corrosive sublimate, some suitable diluent is used that will be completely soluble in water and if possible aid in the solution of the mercuric chloride without reacting with it chemically; for this purpose ammonium chloride or citric acid is commonly used. In some few instances both together have been employed. To prevent the material sticking to the dies on a tablet machine, some lubricant is necessary, and as a comparatively soluble substance, antiseptic in itself, boric acid is often employed in a case of this kind. A quantity of tablets began to evolve considerable amounts of hydrochloric acid gas, sufficient to rapidly attack tinned-iron containers shortly after they were made. It was found that the boric acid used as a lubricant, in the presence of citric acid, reacted upon the ammonium chloride with the evolution of hydrochloric acid. The omission of either the boric or citric acid immediately remedied the trouble.

Another problem that seemed on the face of it so simple that it was really no problem at all was the obtaining of material such as sodium chloride, milk sugar, and alkaloidal salts of such purity that they would give a solution in distilled water *completely free* from insoluble floating particles. I would not go so far as to say that it cannot be done; I think that conditions are conceivable under which it might be accomplished; but I have never seen it done, and upon a commercial scale it has, so far as I know, never been accomplished. You must remember, of course, that the floating particles thus referred to are minute, though easily visible to the naked eye. Some years ago it was desired to prepare C.P. sodium chloride in crystalline form suitable for redissolving in distilled water for intravenous injection. No sodium chloride of sufficient purity was obtainable on the market, and in attempting to make a quantity, it was found that during evaporation in a carefully purified solution, the sodium chloride would attack tinned copper, aluminum, and several grades of special enameled iron to such an extent that the crystals when redissolved in water would show a weighable

amount of insoluble matter. The best thing available was one particular grade of resistant enamel, though had it been available on a commercial scale, a pure silver pan would probably have been just as effective.

When it comes to milk sugar or alkaloidal salts, it would seem that all that is necessary is to carefully filter the solution and evaporate, to obtain a product that will redissolve in distilled water without showing any signs of floating particles. When you come, however, to critically examining such solutions, you will discover that the first thing is to get distilled water which under the most rigid tests will show no tiny particles floating in it. So far I have never seen any of the above mentioned substances or distilled water that would show absolutely no signs of tiny floating particles when viewed by the naked eye against a dark background under an electric light. Remember, though, that one liter or even five liters of such a solution will leave no weighable residue on a filter paper; in fact, unless the filter is hard and smooth it is very likely to make the solution worse.

After problems connected with the manufacture are solved, there come up also numerous questions in regard to containers used. For example, glass that contains any trace of alkali soluble in water (and this is the rule rather than the exception) cannot be used in making ampoules containing very delicate substances, for strychnine alkaloid will be precipitated from its salts and a delicate organic preparation like adrenalin will be quite rapidly destroyed. Containers made from coke tin plate cannot be used to hold materials that might slowly attack iron, whereas charcoal tin plate is satisfactory, the difference being that the former has occasional exceedingly minute holes through the tin, while in the latter the tin coating is uniform and unbroken.

When we come to the consideration of the more difficult problems connected with medicinal substances and their development we reach a vast unknown region that has been but most imperfectly explored. We speak glibly oftentimes of relationship between chemical constitution and physiological action, but our actual and definite knowledge of the relationship is at the best extremely limited. We have acquired what seems like a considerable amount of empirical understanding that certain effects are in some way associated with certain combinations of elements or radicals, but we may draw a hasty conclusion merely to find that there are numerous exceptions

to our supposed "law." For example, pyrocatechol (ortho-dihydroxy-benzene) is more poisonous than its monomethyl derivative, guaiacol, which in turn is more potent than the dimethyl derivative, veratrol. Apparently we are on the road to prove that alkylation of a hydroxy group in aromatic compounds decreases the toxicity, but presently we find that from resorcinal, which is meta-dihydroxy-benzene, we obtain a dimethyl derivative that is very much more toxic than the parent substance and our interesting theory suffers a rude shock.

If now we cautiously advance along some of the blazed trails in the jungle of organic compounds, hoping fervently that harsh and unrelenting facts will not pounce upon and tear to pieces some of our nicely domesticated pet theories, we discover some rather astonishing things. Take adrenalin, which, as derived from its natural source, is levorotatory. When prepared synthetically it is racemic and much less active than the naturally occurring form. Further investigation shows that the dextrorotatory form is only about one-twelfth as powerful in increasing the blood pressure as the levorotatory form. The peculiar effect of the atropine group of alkaloids in dilating the pupil of the eyes is about fifteen times as great in levohyoscyamine as in its stereoisomer. Atropine and cocaine are not widely different chemically, both being derivatives of the nucleus tropine, but while some points of likeness may be found in their physiological action, there are many and pronounced differences, for instance, cocaine is a powerful local anesthetic, while atropine is devoid of this effect. Again, cocaine is methyl-benozyl-ecgonine and ecgonine has no local anesthetic properties, while neither benzoyl-ecgonine nor ecgonine-methyl ester have more than a very slight effect of this kind. And so we go, gradually accumulating a great store of isolated facts and laboriously fitting them together. We are very like the child with a jig-saw picture puzzle: we fit together a few facts here and a few more over there and occasionally have to take apart some which do not fit perfectly, hoping that some day we will get enough of this picture together to find out what it really looks like.

Turning for a moment to other questions, how shall we determine the medicinal activity of aconite preparations? The drug contains one important and highly toxic alkaloid, aconitine, but also varying amounts of related alkaloids which are not only much less toxic but in some cases actually antagonistic in their action to the aconi-

tine. The aconitine itself is very easily affected by heat, especially in the presence of moisture, and decomposes into various other bodies which possess quite different physiological action. One can obtain concordant results on repeated chemical assays, and find that they fail entirely to agree with the physiological activity as determined by tests on animals. Both the physiological tests and the chemical assay seem to be affected by the presence of secondary alkaloids. The present situation as regards the determination of the activity of aconitine preparations is in a very unsatisfactory state.

For over 100 years we have known that the most important alkaloid of opium is morphine, but only within the past 10 years have we come to a definite understanding of its chemical constitution, and though at present morphine is worth $200 per pound, there is no commercially available process for producing it synthetically.

Then there is that class of substances known as enzymes, typified among medicinal agents by pepsin, pancreatin, and diastase. We have for years used these products, particularly pepsin, as an aid to imperfect digestive activity, but do not yet know their exact constitution. Most extensive investigations have been pursued regarding the nature of pepsin, and it has been possible to produce a material under this name of such strength that one part will digest 50,000 parts of coagulated egg albumin, showing a tremendous power of protein digestion. Even here apparently the limit is not reached, and we have not succeeded in isolating any definite substance whose chemical identity we can establish.

Pancreatin is known to be a mixture of several different enzymes, but we are no better acquainted with the constitution of any of them than we are with that of pepsin. Besides these substances there are numerous other enzymes of more or less importance that occur either in vegetable or animal life, and many of which undoubtedly have important rôles to play in connection with vital processes, and as we come to understand them better we may find some of them of great service in dealing with diseases that are now but imperfectly understood.

In investigating enzymes we are struck with the similarity in many respects between catalytic action of these organic substances and those inorganic colloidal solutions of metals that are quite extensively advocated as remedial agents. For instance, both are rendered inactive by boiling and are affected by the reaction of the

medium in which they act. The decomposition of hydrogen peroxide by catalase, which reaction may be used for the quantitative determination of this enzyme in the blood or liver, or the similar decomposition by colloidal solution of platinum, both proceed more rapidly in a slightly alkaline medium. The presence of a trace of hydrocyanic acid acts as a distinct poison, and inhibits the activity both of enzymes and colloidal solutions, though there are some exceptions to this rule. What is the chemical reason back of these resemblances between substances that seem otherwise so dissimilar?

One of the scourges of humanity in Eastern Asia, the Philippines, Borneo, Sumatra, and the Straits Settlement has been a disease known as beri-beri. This through long and laborious investigations was found to be connected with the type of food used, being especially prevalent where polished rice was the main article of diet. It was found that a very remarkable and rapid improvement in the condition of those afflicted with this disease could be produced by extracts from the husks and polishings removed from rice. Continued investigation has led to recognition of certain bodies called "vitamines" present not only in the pericarp of rice but also in other grains, in yeast, and in a number of different plants. The name has been given because it is known that these substances are related to the amines and are so intimately associated with vital processes. They are present in only exceedingly minute amounts and yet their effect is very great. To the presence or absence of the same compounds has been traced the disease quite prevalent in our own southern states, known as "pellagra."

We are just beginning to understand that these vitamines, which all these years we have taken into our systems with our daily food, have in some way a tremendous effect upon our health, but how widely they are distributed or what their chemical constitution is and how they may differ as derived from different sources, and why they are so necessary to our healthful existence, still remains almost a complete mystery. Few, if any, greater fields for chemical investigation of medicinal substances exist at present than that of the vitamines.

Some 400 years ago Paracelsus founded what came to be known as the School of Iatrochemistry, on the assumption that the human body was made up of chemical substances and that illness was caused by chemical changes in the organs and juices of the body, and that to cure these ills chemical compounds must be found that

would restore the original healthy condition. This fundamental principle was so obscured by fantastic ideas and was carried to such extremes by overzealous followers that it fell into disrepute and finally disappeared entirely, giving place to a chemistry founded on careful experimentation rather than fanciful theories. Strangely enough we are now returning, but under very different auspices, the limitations of our knowledge and the fact that we must not be too eager to draw conclusions from the isolated facts we know, but as in former days the practice of pharmacy and the art of healing did much to develop chemical knowledge, so to-day must chemistry in its fullest application go far toward improving our means of treatment and control over disease.

PARKE, DAVIS AND COMPANY,
DETROIT, MICH.

THE TRADE IN CINCHONA BARK.[1]

BY B. F. HOWARD.

An article on "The Future of the Trade in Cinchona Bark" appearing in the last issue of the *Bulletin of the Imperial Inst.*[2] contains much information of value to those who desire to have an authoritative résumé of this important subject.

An interesting introduction traces briefly the history of the natural Cinchonaceæ of the forests of the Andes, and the botanical classification of the varieties best known on the market at the present day. Turning to the production of cultivated bark, the author gives the output in recent years from the plantations in the Dutch East Indies, India and Ceylon, and shows clearly the enormously important part played by the Dutch plantations in Java. In recent years, Java heads the list of producers with an annual output of 22,880,000 lbs., India supplying 2,000,000 and other countries 440,000 lbs. Perhaps these figures should be taken as a general indication of the preeminence of Java rather than as an exact comparison, for whereas the Java production is based on an average of the years 1911–1913, the Indian output given is the average of the years 1912–1913 to 1915–1916, and this must surely have been affected by the difficulties of production and shipping during the war.

[1] Reprinted from *Jour. Soc. of Chem. Industry*, February, 1919.
[2] XVI, Pt. 3, 1918.

The commercial or market aspect is then briefly dealt with and the efforts—successful in the main—described which were adopted to prevent over-production in the years before the war. Under a heading entitled "Trade in Cinchona Bark and Quinine," the author shows that although the Indian plantations and factories are unable to supply the needs of that portion of the Empire, yet the bulk of the imports of manufactured quinine into India have hitherto been from British sources.

A series of import and export tables follows showing the high percentage of the quinine requirements of the United Kingdom which was formerly supplied by Germany—a typical example of the position of the fine chemical industry in this country before the war, and a state of affairs which, we trust, has now gone for ever.

The great importance of local manufacture of quinine salts in Java and its possible future bearing on the world's quinine trade is not mentioned, probably owing to the complexity of the problem and the difficulty of obtaining accurate information. It is obvious, however, that no account of the cinchona industry which ignores this important factor can be considered complete.

The final portion of the article deals with bark produced in St. Helena and East Africa. Although from a commercial point of view these plantations are at the moment negligible, yet from the scientific aspect the typical analyses given are of considerable interest as they show a high percentage of quinine and prove the bark to be well up to the Java standard, thus indicating most successful cultivation—which may have been either deliberate or accidental. Viewed in detail the tables giving the results of examination of these barks appear to be somewhat inadequate and to lack uniformity. Although the total alkaloid figure and the percentage of quinine sulphate are given, a complete separation of the four principal alkaloids has apparently not been attempted. Again, the results are complicated by the inclusion of the percentage of moisture found, but as bark is valued on its alkaloid contents as shipped, moisture is not a factor of any importance. A more practical method of stating the results would be to give the percentage of (hydrated) sulphate of each of the alkaloids (quinine, cinchonidine, quinidine and cinchonine), together with the percentage equivalent of alkaloid in each case; also the sum of these figures and the amount of amorphous alkaloid. So tabulated, the results of the analyses of these very interesting samples would have enabled the

reader to evaluate the barks commercially, as well as to derive useful additional scientific information from them.

[Contribution from the Research Laboratory and the Department of Glandular Extracts, Parke, Davis & Co.]

STUDIES ON PEPSIN. I. CHEMICAL CHANGES IN THE PURIFICATION OF PEPSIN.[1]

By Lewis Davis and Harvey M. Merker.

The question of the chemical composition of pepsin has occupied the attention of a number of investigators. Following the classical researches of Pawlow[2] and his pupils, Pekelharing[3] appears to have been the first to undertake purification of the enzyme. This investigator prepared a light yellow powder which, while readily soluble in dilute acids and sodium chloride solution, dissolved with difficulty in water but showed strong peptic activity. It gave reactions for albumin, but was believed to contain a soluble phosphorus compound as an impurity. On boiling pepsin solutions, Pekelharing obtained a nucleoproteid and was able, under certain conditions, to separate an albumose.

Nencki and Sieber,[4] using as initial material juice obtained through gastric fistula in dogs, claim to have secured an active pepsin preparation through precipitation which is free from albumin. At the same time, they consider the precipitate of transparent granules containing chlorine which they obtained by strongly cooling the gastric juice to be a chemical individual, and, in all probability, the true enzyme. They also submit analyses to support their contentions. Pekelharing,[5] in a later investigation, in which he employed the artificial gastric juices extracted from several hundred hog stomachs by his previous method, and also the juice obtained from gastric fistula in dogs, disproved this view. He found pepsin

[1] Read before the Biological Section of the American Chemical Society at the Cleveland meeting, September 12, 1918. Reprinted from *The Journal of the American Chemical Society*, February, 1919.

[2] Pawlow, *Centr. Physiol.*, 1888; *Ergebnisse Physiol.*, 1902, i, Part I, 246.

[3] Pekelharing, *Z. physiol. Chem.*, vol. 22, 233, 1897.

[4] Nencki and Sieber, *ibid.*, vol. 23, 291, 1901.

[5] Pekelharing, *ibid.*, vol. 35, 8, 1902.

to be free from phosphorus and to contain no nucleoproteid, but the analyses of his preparations showed no constancy in results.

That a protein-free pepsin solution having digestive action is possible, has also been maintained by Schrumpf.[6] The latter prepared a Büchner-pressed extract of hog stomachs, clarified by filtration, and dialyzed against running water. The dialysate thus obtained was precipitated by addition of cholesterin in alcohol-ether solution, filtered, the precipitate redissolved in water, and the suspension finally clarified by a Kitasato candle. The clear filtrate, while giving none of the protein reactions, still showed powerful digestive activity.

The amino acid constituents of pepsin have been investigated by Hugounenq and Morel[7] using an autodigested, hydrochloric extract of hog stomachs. They conclude that an extract of pepsin contains a number of monoamino acids in the free state, probably formed in the autodigestion. Glycocoll, aspartic and glutaminic acids, and also histidin, they found to be absent in the material examined.

It is thus readily apparent that, as true with other enzymes, the chemical nature of pepsin is still an open question. Nearly all of the above investigators have based their conclusions on crude preparations, undoubtedly containing admixed or combined impurities. Seemingly, no attempt has been made to prove, by quantitative measurements of the proteolytic activity, that an actual purification has taken place, where such is mentioned. The present investigation was undertaken by us to determine what changes take place in the purification of pepsin, with the view of possibly throwing some light on the chemical nature of the enzyme.

Experimental Procedure.

Methods.—As basic material for purification, a composite lot (consisting of a number of different samples) of 1:2,000 commercial pepsin was employed. Sufficient stock of this mixture was reserved to enable the preparation of all of the various strengths of the enzyme given below. The weaker samples (up to 1:18,000) were prepared by fractional precipitation of a 20 per cent. aqueous solution, while the more active strengths were obtained by salting out the former, filtering and dialyzing. In each case, the final

[6] Schrumpf, *Beitr. Holm.*, vol. 6, 396, 1905.

[7] Hugounenq and Morel, *Compt. rend.*, vol. 147, 212, 1908.

purified material was dried to a constant moisture content of about 5 per cent. and scaled. Assays for proteolytic power were then carried through and the samples analyzed chemically.

Determination of the proteolytic strength of the different samples, made in association with our colleagues, L. M. Gerdes and W. L. Seibert, was in accordance with the method given in the ninth revision of the U. S. Pharmacopœia.[8] The assays were checked in each case, and controlled by running through a standard (1:3,000) pepsin under identical conditions.

The chemical examination included analyses of total mineral matter, total nitrogen, total sulphur by the method of Wolf and Osterberg[9] volumetric estimation, in the ash, of phosphoric acid as P_2O_5,[10] chlorides as NaCl,[11] calcium as CaO; also, determination of nitrogen existing in coagulable protein, proteoses by zinc sulphate precipitation,[12] peptones by Bigelow and Cook's[13] modification of Sjerning's method, and amino acids according to Van Slyke.[14] In addition, observations were made in a 2 per cent. aqueous solution of optical rotation, and of the hydrogen-ion concentration. The direct reading ionometer described by Bartell[15] was used in the latter, with a Weston Standard Cell, and the chain: Calomel electrode (*N* KCl)—saturated KCl—pepsin solution—Pt. electrode—H_2 at 23°. The complete "set up" employed was similar to that used by Davis[16] in a previous investigation of diphtheria toxin.

Supplementing the preceding, qualitative tests were carried out in accordance with the technique employed by one of us, Davis,[17] with peptone samples. Both a straight 2 per cent. aqueous solution and the filtrate, after coagulating the protein, were used, and examination made for: tyrosin (xanthoproteic, Millon's reaction)

[8] "Pharmacopœia of the United States," 1916, p. 312, 9th rev., P. Blakiston's Son & Co.

[9] Wolf and Osterberg, *Biochem. Z.*, vol. 29, 429, 1910.

[10] "Methods of Analysis, A. O. A. C.," U. S. Dept. Agr., Bur. Chem., *Rev. Bull.*, 107, 4, 1912.

[11] "Standard Methods of Water Analysis," *Am. Pub. Health Ass'n*, 1917, p. 4.

[12] Bömer, *Z. anal. Chem.*, vol. 5, 562, 1895.

[13] Bigelow and Cook, *Journal of the American Chemical Society*, vol. 38, 1496, 1906.

[14] Van Slyke, *J. Biol. Chem.*, vol. 16, 121, 1913.

[15] Bartell, *Journal of the American Chemical Society*, vol. 39, 630, 1917.

[16] Davis, *J. Lab. Clin. Med.*, vol. 3, 358, 1918.

[17] Davis, *ibid.*, vol. 3, 75, 1917.

TABLE I.

Analyses.

Proteolytic, strength (U. S. P. IX.)	Total Mineral Matter, %.	Phosphoric Acid as P_2O_5 %.	Calcium as CaO, %.	Chlorides as NaCl, %	Total Sulphur, %.	Percentage of Nitrogen in					Optical Rotation α_D at 24°.	Reaction C_H + at 23°.
						Total, %.	Coagulable Protein, %.	Proteoses, %.	Peptones, %.	Amino Acids, %.		
1:2,000	5.37	1.58	0.26	1.19	0.63	12.93	1.15	0.73	7.37	4.39	−2° 58′	.....
1:5,500	4.31	1.42	0.32	Trace	0.70	12.60	1.41	1.76	4.78	4.04	−2° 0′	.....
1:6,000	3.34	1.03	0.46	Trace	0.81	13.41	1.43	2.10	4.91	3.15	−2° 6′	.....
1:10,000	3.31	1.42	0.35	Trace	0.89	13.55	1.63	3.00	3.73	3.09	−2° 24′	.....
1:12,000	2.31	1.28	0.29	Trace	0.63	12.95	2.33	3.09	3.41	2.75	−2° 10′	.....
1:18,000	2.84	1.47	0.71	Trace	1.50	13.47	3.16	3.62	2.68	2.10	−2° 30′	.....
1:21,000	2.38	1.29	0.58	Trace	0.82	12.57	3.69	3.91	3.73	1.45	−2° 0′	.....
1:24,000	2.84	1.27	0.52	Trace	0.77	12.64	3.98	4.10	0.96	1.35	−2° 4′	2.5×10^{-4}
1:28,000	1.86	1.09	0.53	None	1.62	13.72	4.39	4.32	0.78	1.22	−2° 20′	4.0×10^{-5}
1:40,000	2.01	0.47	1.01	None	1.50	13.77	8.34	4.43	..	0.61	−2° 30′	6.0×10^{-7}

TABLE II.

Reactions in 2 Per Cent. Solution.

Proteolytic Strength. (U. S. P. IX.)	Character of Solution.	Picric Acid Reaction.	Ammonium Sulphate Reaction.	Millon's Reagent.	Biuret Reaction.	Hopkins-Cole Reagent.	Molisch s Reagent.	Xanthoproteic Reaction.
1 : [illegible],000	Straight			Mod. ppt., reddish	Bluish pink	Ppt., ring	Ppt., ring	Yellow color ppt., orange
	Coag. filtrate	Mod. ppt.	No ppt.	Sl. ppt., reddish	Bluish pink	No ppt., ring	Ppt., ring	Yellow, deep orange
1 : 5,500	Straight			Heavy ppt., pink	Bluish pink	Ppt., ring	Ppt., ring	Ppt., orange
	Coag. filtrate	Mod. ppt.	No ppt.	Sl. ppt., reddish	Bluish pink	No ppt., ring	Ppt., ring	No ppt., mod. orange
1 : 6,000	Straight			Mod. ppt., pink	Bluish pink	Ppt., ring	Ppt., ring	Ppt., mod. orange
	Coag. filtrate	Mod. ppt.	No ppt.	Sl. ppt., pink	Bluish lavender	No ppt., ring	Ppt., ring	No ppt., deep orange
1 : 10,000	Straight			Heavy ppt., pink	Bluish pink	Ppt., ring	Ppt., ring	Ppt., deep orange
	Coag. filtrate	Mod. ppt.	No ppt.	Sl. ppt., pink	Bluish lavender	No ppt., ring	Ppt., ring	No ppt., light orange
1 : 12,000	Straight			Heavy ppt., pink	Bluish pink	Ppt., ring	Ppt., ring	Ppt., orange
	Coag. filtrate	Mod. ppt.	No ppt.	Sl. ppt., pink	Bluish lavender	No ppt., ring	Ppt., ring	No ppt., light orange
1 : 18,000	Straight			Heavy ppt., reddish	Bluish pink	Ppt., ring	Ppt., ring	Ppt., orange
	Coag. filtrate	Mod. ppt.	No ppt.	Sl. ppt. pink	Bluish lavender	No ppt., ring	Ppt., ring	No ppt., red-orange
1 : 21,000	Straight			Heavy ppt., pink	Bluish pink	Ppt., ring	Ppt., ring	Ppt., red-orange
	Coag. filtrate	Mod. ppt.	Sl. opal	Sl. ppt., red tinge	Bluish lavender	No ppt., ring	Ppt., ring	No ppt., orange
1 : 24,000	Straight			Heavy ppt., pink	Bluish pink	Ppt., ring	Ppt., ring	Ppt., red-orange
	Coag. filtrate	Sl. ppt.	Sl. opal	Sl. ppt., red tinge	Bluish lavender	No ppt., ring	Ppt., ring	No ppt., yellow-orange
1 : 28,000	Straight			Heavy ppt., pink	Bluish lavender	Ppt., ring	Ppt., ring	Ppt., red-orange
	Coag. filtrate	Sl. ppt.	Sl. opal	Trace ppt., red tinge	Bluish lavender	No ppt., trace ring	Ppt., ring	No ppt., faint reddish
1 : 40,000	Straight			Heavy ppt., pink	Bluish ppt., lavender	Ppt., ring	Ppt., ring	Ppt., red-orange
	Coag. filtrate	Opal	Opal	Opal red tinge	Bluish, no color	No ppt., no ring	Ppt., ring	No ppt., faint reddish

tryptophane (Adamkiewicz Hopkins-Cole reagent), glycoprotein and glycoproteose (Molisch reagent). Tests were also made on the filtrate from coagulable protein, for proteoses (by addition of saturated zinc sulphate, ammonium sulphate, picric acid solutions), and protoproteoses (by saturated sodium chloride solution, potassium ferrocyanide in acetic acid solution).

Results.—Altogether, nine purified products were prepared. Including the basic pepsin material, the various proteolytic strengths of the enzyme which were examined ranged from 1:2,000 to 1:40,000 (U. S. P. IX). The results given in the accompanying Tables I and II, are, in every case, based on duplicate determinations and, because of possible variation in the U. S. P. pepsin assay, these estimations were carried out in triplicate by two different observers.

As may be noted from Table I, the purification of pepsin is accompanied by a general decrease in the total mineral matter. This ranges from an ash content of nearly 5.5 per cent., in the case of the basic (1:2,000) product down to about 2 per cent. with the highest proteolytic strengths obtained. The phosphoric acid content, also, shows a gradual decrease so that the value at 1:40,000 is less than one third that of the basic material. Both the calcium oxide and total sulphur values fluctuate in the different strengths, but both show an increase in the purified as compared with the unpurified samples. It is a significant fact that the chlorides, which are present to the extent of 1.19 per cent. (as NaCl) in the 1:2,000 sample, practically disappear as a result of purification.

Probably the most important data are furnished by the various nitrogen factors, particularly the nitrogen in amino acid condition. Confirming more elaborately the results found by Aldrich,[18] there is found to be almost a uniform decrease in α-amino acid nitrogen so that in the sample testing 1:40,000 only 0.61 per cent. is found. Corroborating these results, it will be noted from the table that there are steady increases in both the coagulable protein nitrogen and that existing as proteoses, while the peptone nitrogen like that of the amino acids shows a decrease. The values for total nitrogen showed decided variations among the different samples with no significant change as the purification increases.

All of the different strengths of the pepsin examined show levorotation in very nearly the same degree, so that this factor is apparently unaltered as a result of purification. With the exception

[18] Aldrich, *J. Biol. Chem.*, vol. 23, 339, 1915.

of the strongest sample obtained (1:40,000) a slight amount of hydrochloric acid was used in the preparation of the other strengths of the pepsin. As a consequence, 2 per cent. aqueous solutions of these samples show relatively high hydrogen-ion concentration. However, the reaction of the 1:40,000 sample, which is the nearest approach to the pure enzyme, is very nearly neutral ($C_{H^+} = 6.0 \times 10^{-7}$). This would tend to disprove the view held by Jacoby[19] and others that pepsin is an acid.

Consideration of the data presented in Table II shows that the results corroborate, in a general way, the analytical data already discussed. No tests were made on the straight pepsin solutions with saturated picric acid, sodium chloride and ammonium sulphate solutions, and also none with potassium ferrocyanide in acetic acid solution, since the results with all of these reagents, because of coagulable protein would be positive, and practically the same for the different strengths. Confirming the results given in Table I, the saturated picric acid; Hopkins-Cole, and Millon's reagent tests, made of the filtrate after removal of coagulable protein, show presence of amino acid and peptid bodies in the lower strength samples. These gradually disappear so that only traces are found in the highest strength sample of the enzyme. Both saturated sodium chloride solution and potassium ferrocyanide in acetic acid solution gave negative results, indicating absence of protoproteoses in the filtrate from coagulable protein. A positive reaction was obtained in every case with Molisch reagent showing presence of glycoprotein, or its derivatives, in the material. It is significant that the biuret test of the filtrate after coagulation of protein in the 1:40,000 sample, is negative. This would indicate that practically all of the protein material is of the nature of coagulable protein or even more complex in its protein character.

Discussion.

A review of the data presented in the foregoing seems to show that in the purification of pepsin there is a gradual elimination of the secondary protein derivatives including amino acids. This is manifested by a constant tendency in the purified samples to approach nearer to the actual character of proteins with increasing proteolytic activity, and is accompanied by an increase in material coagulable by

[19] Jacoby, *Biochem. Z.*, vol. 4, 471, 1907.

heat. From the fact that the highest strength samples still give strong tests with Molisch reagent, it may be possible that the pure enzyme is a conjugated protein, probably a glycoprotein.

Confirming this view, the mineral matter is decidedly less in the purified samples than in the original basic material, approaching almost to the value for pure proteins in the case of the strongest samples. Both sulphur and calcium are probably unaffected by the purification, but there is a decided decrease in the phosphorus content and seemingly a total elimination of chlorides. Other than the increase which would obtain by removal of non-nitrogenous impurities, there is probably not much change in the content of total nitrogen as a result of pepsin purification.

The manner in which the α-amino acids decrease as the proteolytic activity increases is striking, and seems to be almost proportional in amount. It is noteworthy that the small amount of α-amino acid present in the sample tesing 1:40,000 (0.61 per cent.) very nearly approaches the value for this factor due to lysin as found present by Van Slyke and Birchard[20] in most proteins analyzed by the nitrous acid method.

Results of optical activity determinations are apparently of no significance, since the same values are obtained with several different strengths of pepsin. As already mentioned above, the reaction in aqueous solution of the strongest (1:40,000) pepsin is significant because of its very slight acidity. It would seem very likely, that the concentration of hydogen ions in solutions of the pure enzyme, when isolated, will probably show only the slight acidity comparable to that given by other proteins.

In connection with the assays of proteolytic strength by the U. S. P. method, it was deemed of interest to make a comparison of the rennetic power of the different samples. It is a significant fact that throughout the entire series, from 1:2,000 to 1:40,000, the rennetic activity and proteolytic strengths are found to go hand in hand. This is being investigated, and will be reported upon in a later paper.

Conclusions.

1. The purification of pepsin seems to consist in the elimination of secondary protein derivatives including α-amino acids.

2. Calcium and sulphur appear to be unaltered as a result of

[20] Van Slyke and Birchard, *J. Biol. Chem.*, vol. 16, 539, 1914.

purification, but phosphorus is materially reduced. Chlorides are seemingly entirely removed.

3. Aqueous solutions of pepsin, after purification, show no material change in optical activity. A sample of high digestive power (1:40,000), shows a reaction very nearly neutral.

4. Pepsin tends to approach nearer to the actual character of a protein (possibly a glycoprotein) with increasing proteolytic activity.

DETROIT, MICHIGAN.

THE ESTIMATION OF PHENACETIN AND OTHER PARA-AMINOPHENOL DERIVATIVES OF HYPOCHLOROUS ACID.[1]

BY A. D. POWELL.

The estimation of the substituted phentidine compounds used in medicine, either alone or in admixture with other substances such as salol and caffeine, has always presented certain difficulties, and various methods have been proposed in recent years for the analysis of mixtures of these substances. Several of these are based on the varying solubilities of the compounds in organic solvents, a more or less complete separation being made, and the separate substances determined gravimetrically. Thus, Seidell[2] proposed a method of this type for the estimation of acetanilide, phenacetin, etc., in "headache powders." Emery, Spencer, and Le Febvre,[3] for the estimation of phenacetin and salol, make use of selective hydrolysis, finally reconverting the phenetidine to phenacetin by acetylation, and weighing the phenacetin as such, the salol being estimated by bromine absorption. Another method recently published by Salkover[4] for the separation of these drugs depends on the solubility of salol in petroleum ether, phenacetin and acetanilide being nearly insoluble in this solvent.

Such methods suffer from the obvious defect that they do not sufficiently identify the substances present in the mixture, and the melting-points of the separated constituents cannot always be relied on, owing to the separation not being perfect.

[1] Reprinted from *The Analyst*, January, 1919.

[2] *J. Amer. Chem. Soc.*, 1907, 29, 1088–1091; *The Analyst*, 1907, 32, 360.

[3] *J. Ind. and Eng. Chem.*, 1915, 5, 681–684; *The Analyst*, 1915, 40, 445.

[4] *Amer. J. Pharm.*, 1916, 88, 484–485; *The Analyst*, 1917, 42, 16.

Methods taking into account the chemical constitution of these compounds have also been proposed. Taylor and Vanderkleed,[5] for instance, estimate phenacetin and acetanilide (individually), by steam distillation and titration of the acetic acid produced on hydrolysis. Another method proposed by Emery[6] for the separation and estimation of phenacetin and acetanilide depends on the property of phenacetin of combining with iodine to form an insoluble periodide, acetanilide either not reacting with iodine or producing a soluble compound. The amount of iodine precipitated from solution is determined by titration of the excess left in solution, and the phenacetin content calculated from the figures thus obtained. An iodimetric method for the estimation of phenolic compounds has been published by Wilkie;[7] but this does not appear to have been extended to the aminophenols and phenetidins, although it seems probable that such compounds might form definite iodo-derivatives.

As far as my own experience goes, however, no method has been published in which any characteristic reaction of *p*-phenetidine or *p*-aminophenol has been taken as the basis for the estimation of this group of compounds. The reactions of *p*-aminophenol with oxidising agents were therefore investigated, in order to determine which, if any, could be made the basis of a quantitative estimation. Oxidation by means of potassium dichromate to form quinone was tried, but was found unsatisfactory, as part of the *p*-aminophenol was converted to quinhydrone. The reaction between sodium hypochlorite and an acid solution of *p*-aminophenol was found to be much more promising. These substances react in accordance with the equation:

$$OH \cdot C_6H_4 \cdot NH_2HCl + 4Cl = O : C_6H_4 : NCl + 4HCl,$$

the quinone chlorimine precipitating as golden-yellow flocks from concentrated solutions, but remaining in solution at dilutions below about 1 per cent.

P-phenetidine is also converted to quinone chlorimine by the action of hypochlorous acid. The reaction is quantitative, and provides a rapid means for the estimation of these bases and all their derivatives which yield the free base on hydrolysis.

The direct absorption of chlorine does not form a suitable basis

[5] *Amer. J. Pharm.*, 1907, 79, 151–156; *The Analyst*, 1907, 32, 215.
[6] *J. Ind. and Eng. Chem.*, 1914, 4, 665–669; *The Analyst*, 1914, 39, 433.
[7] *J. Soc. Chem. Ind.*, 1911, 30, 398; *The Analyst*, 1911, 36, 294.

for calculating the results, owing to the difficulty of determining when an excess has been added, and it is therefore necessary to determine the amount of quinone chlorimine formed, after addition of excess of hypochlorite and removal of free chlorine from solution. In the absence of free chlorine, the reaction between the quinone compound and hydriodic acid affords a convenient means of determining this. The reaction is the reverse of that given above, four atoms of iodine being liberated by each molecule of quinone chlorimime, and *p*-aminophenol being re-formed.

As no reagent was found which will combine with the excess of free chlorine without also decomposing the chlorimine, and boiling is out of the question owing to the volatility and instability of the latter in hot solutions, the chlorine must be removed by blowing a current of air through the solution. Experiments showed that chlorine is fairly rapidly removed by this means, 100 Cc. of a saturated aqueous solution of this gas losing 98 per cent. of its strength after five minutes aëration at the rate of 700 to 800 Cc. of air per minute, and becoming practically free from chlorine after fifteen minutes. The quinone chlorimine being also slightly volatile, and tending to decompose on long standing in acid solution, it is necessary to add a small correction to account for this. Any error introduced by the action of the dissolved air on the iodide subsequently added is included in this correction, which averages 1:5 per cent. of the total quinone chlorimine present for an aëration of from fifteen to twenty minutes.

The details of the method finally adopted are shown in the following examples of its application:

Estimated of p-Aminophenol, p-Phenetidine, etc.—An amount of an acid solution equivalent to about 0.1 Gm. of the base is measured into a 250 Cc. stoppered bottle and diluted to rather more than 100 Cc.; 5 Cc. of strong hydrochloric acid are added, followed by 10 Cc. of sodium hypochlorite solution (about 0.8 N). The resulting solution should be pure yellow, and not deposit yellow flocks. Air is now blown through at a brisk rate for fifteen minutes, in which time all chlorine will have been removed, 2.5 Gm. of potassium iodide are added, and the solution allowed to stand for at least five minutes, as the reduction is rather slow. The liberated iodine is then titrated with $N/10$ thiosulphate and starch indicator. Any residual blue tint shows that reduction has not been complete.

Each Cc. of $N/10$ thiosulphate is equivalent to 0.00273 Gm. of

p-aminophenol, or 0,00343 Gm. of *p*-phenetidine. The result is multiplied by the factor 1.015 to correct for loss during aeration.

Estimation of Phenacetin.—One Gm. of phenacetin is boiled for two hours with a mixture of 25 Cc. strong hydrochloric acid (1.16) and 15 Cc. water in a small flask fitted with an air condenser. After cooling, the solution is diluted to some definite volume, and an aliquot representing 0.2 Gm. phenacetin is taken for estimation exactly as above.

Each Cc. of $N/10$ thiosulphate is equivalent to 0.00448 Gm. of phenacetin. A large number of samples of commercially pure phenacetin, examined as above, gave figures ranging from 99.2 to 100.2 per cent.

Estimation of Phenacetin in Admixture.—The following experiments were made on mixtures of phenacetin with caffeine citrate, salol, and acetanilide respectively:

With Caffeine Citrate.—A mixture of 0.8 Gm. phenacetin with 0.4 Gm. caffeine citrate was treated exactly as for phenacetin. The results were slightly high, owing to formation of a small amount of some substance from the caffeine citrate which liberated iodine from hydriodic acid. The percentage of phenacetin calculated out 68.5 and 68.7, instead of 66.7 required by theory. No correction for the volatility of the quinone chlorimine was made in these cases, the error already mentioned more than compensating for loss by this means.

With Salol.—A mixture of equal parts of phenacetin and salol (0.5 Gm. of each) was dissolved in 20 Cc. 10 per cent. sodium hydroxide, and warmed on the steam-bath for fifteen minutes to hydrolyze the salol; 40 Cc. of strong hydrochloric acid were then added, and the mixture boiled for two hours. The hydrolyzed solution was shaken with ether to remove salicylic acid and phenol, and the chlorination and titration carried out in the usual manner. The amount of phenacetin found was 49.3 per cent. It was found necessary to remove the products of hydrolysis of salol before adding the hypochlorite, as the precipitates they formed with this reagent held back chlorine and caused high results to be obtained.

With Acetanilide.—Mixtures of acetanilide and phenacetin cannot be analyzed without first removing the acetanilide, as the aniline produced from this substance forms an oily precipitate which apparently retains free chlorine.

Estimation of other p-Phenetidine or p-Aminophenol Deriva-

tives.—Lactophenin (lactyl-*p*-phenetidine) and salophen (salicylic ester of acetyl-*p*-aminophenol) were both estimated after hydrolysis in exactly the same manner as phenacetin, lactophenin giving 99.3 per cent. and salophen 100.4 per cent., after adding the correction previously mentioned.

Analysis of Photographic Developers.—In addition to the medicinal substances already mentioned, there are severel *p*-aminophenol derivatives largely used in photography as developers, which may be estimated in the same manner. For instance, in a developer of the rhodinal type, the proportion of *p*-aminophenol may be quickly found by direct treatment of the acidified solution, the sulphite present being oxidized by the excess of chlorine added.

In the case of metol (methyl-*p*-aminophenol sulphate) it is interesting to note that, owing to the presence of the methyl group in the amino-group, no chlorination of the latter takes place, although a quinone derivative is formed. The reaction is probably

$$OH \cdot C_6H_4 \cdot NH \cdot CH_3 + 2Cl = O : C_6H_4 : N(CH_3) + 2HCl.$$

Consequently, in the subsequent oxidation of hydriodic acid, only two atoms of iodine are liberated per molecule instead of four, as in the case of *p*-aminophenol. The reaction therefore provides a simple means of distinguishing between metol and "metol substitutes," as all the substitutes that I have examined have proved to be either *p*-aminophenol or *p*-aminocresol salts, none of them showing evidence of the presence of a methyl group substituted in the amino group, when tested by the quinone chlorimine method.

I desire to express by thanks to Messrs. Boots' Pure Drug Co., in whose laboratories the above work was carried out.

AN IODINE FACTORY IN EASTERN SIBERIA.[1]

By Dorothy F. Findlay, M.P.S.,

Vladivostok, E. Siberia.

We came upon it on the edge of a beautiful little bay, about 200 miles north of Vladivostok, surrounded by immense bush-covered hills. Among the vastness of the Siberian scenery the little iodine factory looked very insignificant—a big chimney, a low red brick

[1] Reprinted from *The Pharmaceutical Journal and Pharmacist*, January, 1919.

building, mounds of kelp along the beach, and a distinct medicinal odor in the immediate vicinity. All around on three sides, stretching for miles and miles, hill upon hill, mountain upon mountain, and on the fourth side the ocean. We had come overland, through the big government coal mines of Soo-chan, leaving the mines at daybreak, travelling by talaga (Chinese carts) to the coast. The weekly boat to Vladivostok was due in that night, and we intended returning by her. The little village is quite a center for outward and inward passengers, chiefly farmers taking their cattle and produce into town. There is no accommodation for passengers whatsoever, no hotel, restaurant, or waiting-room. The cattle are all deposited on the beach, and the travellers—Chinese, Koreans and some Russians—squat around. They often wait there for hours, as they must arrive by daylight and the boat seldom gets in before 2 A.M. The village—though it can scarcely be called such—consists of the factory and not more than six Russian houses, the remainder being Chinese and Korean huts.

It was pleasant to find something to while away the hours of waiting. The manager of the factory being away, we were shown round by a post-graduate student, who explained every process to us in voluble Russian. It is not necessary to go into details of the manufacture. Newth gives the same process as the one adopted at this factory; suffice it to say that everything is done on the simplest lines. Chinese junks (sailing boats) go out and rake in the seaweed, which is carried up to the top of the beach, stacked in piles, and burnt on the spot, at a stone's throw from the factory. The ash is wheeled straight into the tanks, lixiviated with water in the usual way. Potassium and sodium salts are also made in these works, but their specialty is the pure element. When we had finished our tour we were taken into the laboratory, a large case was unlocked, and with huge pride four large bottles of pure iodine were taken out, each holding 5 kilograms. I had never seen the beautiful glistening scales in such large quantities. This comparatively small case contained the produce of three weeks' work, but was satisfactory, considering the present price of iodine. The head chemist was an ancient Japanese; Japanese chemistry books lined the book-shelves. It was nearly three years since I had been in a laboratory, and this small one was very homely. I went round reading the formulæ on the bottles of the reagents to see if I remembered them. A volumetric analysis was in process at one bench, the pipette

was full of pot. perman. solution; it brought back pleasant memories of a little room behind the shop of a lady chemist, where I did most of my work for the Minor. But it was getting dark, the assistant manager was waiting to shut up and go home. We had nothing so cheerful to look forward to, and it was coming on to rain.

We took shelter under a rock for some hours, and ate our supper of eggs and stale bread and butter brought with us from the day before. At ten o'clock we were rather wet, and went down to the pier to inquire if the boat was soon due. Nobody knew, which is usually the case in Russia. After hanging round for another hour the postman came down with the news that the boat had not left Vladivostok, and there was something wrong with the engine. Our only way home was by talaga, the way we had come, and no driver would think of starting off in the deluge which was now beginning, the rain coming down in bucketfuls at a time. We rushed to the nearest Korean hut for shelter, and were shown into a tiny room about four yards square, where already about a dozen people were waiting. The place had no ventilation, except the door, and was lighted by a glimmer from an evil-smelling oil lamp. It was unpleasant for us, but far more so for the poor farmers who in many cases had come two or three days' journey with their cattle. Only in Russia would people have taken things so placidly. We ourselves were not in at all a good temper. Those who have only ridden in carts along even the worst English road cannot imagine the discomfort of travelling in Chinese carts. These consist of shafts, four wheels, and some planks of wood laid across the axles. The roads are only rough tracks, full of boulders and ruts; there are many streams to cross, and the bridges usually consist of faggots laid across, and the jolting over these without springs is indescribable, and after the heavy rain the roads would be nearly a foot deep in mud, and we should get splashed up to our necks. It was a weird night: inside—the flickerings of the smelly lamp, the alternate arguings and snorings of the farmers, the pest of all creeping things which soon found their way from the walls on to the nearest human body; outside—the rain pouring down, the neighing of horses, and the lowing of cattle. At 3 A.M. the rain somewhat abated and we managed to persuade a driver to take us as far as a village ten miles on the road. With some difficulty he found his own horses, and we left the stifling atmosphere of the hut for the damp dark air outside, with its slight taint of iodine. We splashed through the

mud to our hard seats, and drove into the darkness of the mountain side.

STROPHANTHUS SEMINA, B.P.[1]

By E. M. Holmes, F.L.S.

The commercial history of the strophanthus seed of commerce since its introduction into medicine in 1886, was given by me in 1896,[2] and it was then pointed out that the seeds met with in commerce were invariably mixed with the seeds of other species in varying proportions, and that the seeds of *Strophanthus Courmontii* and its varieties were practically impossible to separate by the naked eye, so that unless the seeds were sent in pods it would be impossible to comply with the Pharmacopœia directions, and use the seeds of *S. Kombe* only.

But although these facts were published in 1906, and illustrations of the difference in the leaves and flowers and seeds of *S. Courmontii* were given with *Pharm. Journ.*, 4, XII., p. 486, the B.P. did not in 1914 direct that the seeds should be kept in their pericarps until required for use, as is ordered in the case of cardamom seeds. For some years past it has been impossible to obtain pure seed of *S. Kombe* in commerce.

The objection has been raised by drug brokers that the weight of the pods adds much to the freight, and that the buyers object to giving more than 3s. 6d. per lb. for the seeds of *S. Kombe,* because other strophanthus seeds can be bought at that price. (But the first importation was entirely of pods, and was purchased by Messrs. Burroughs and Wellcome at a good price.) The result has been that a large number of strophanthus seeds of various species and of unknown medicinal properties have entered into commerce and have been sold as "strophanthus" seeds, dealers being apparently satisfied if there are enough Kombe seed mixed with them "to swear by," and in some cases purposely mixing different lots. The danger of this carelessness about one of the most valuable heart remedies, when given in a proper dose, but which is also a dangerous heart poison in too large a dose, is leading to results that might easily prove disas-

[1] Reprinted from *The Pharmaceutical Journal and Pharmacist*, January, 1919.

[2] *Pharm. Journ.*, 4, XXII, p. 312.

trous. During last week a pharmacist asked me for an opinion on a case that came within his daily work. A patient brought in a prescription of a London physician, ordering ***three times the maximum dose*** of the B.P. tincture (without any indication that the physician was aware of the fact). The chemist hoped to be able to telegraph to the doctor, and made an excuse that it would take time to prepare, but the customer said he must have it at once, as it was a severe case of heart disease and the dose was wanted immediately. The chemist had to consult a neighboring doctor, who advised him not to give more than the maximum B.P. dose.

It is quite obvious that if one pharmacist (retail or wholesale) has a different sample of seed to work with, there is no certainty under present conditions that the same prescription prepared at different shops will be of the same strength, and the relief that the medical man has a right to expect for his patient cannot be depended upon.

The question of price of the seed ought not to enter into the question. In the case of powerful drugs like strophanthus, aconite, and digitalis, used for serious diseases requiring prompt measures, it is important either that the Food and Drug Act should be strictly applied to punish those using adulterated or mixed samples, or that a government inspector of vegetable drugs should be appointed to prevent such important remedies, if adulterated or diluted with other species, from entering into commerce. In view of the limited geographical range of *S. Kombe,* it might be well to order the use of *S. hispidus* instead, as it is much more widely spread and more easily obtained, and is the only other known species that gives the green reaction of sulphuric acid with strophanthus seed, indicating the presence of strophanthin.

Aconite, which affords a similar instance of possible danger to patients, has already fallen somewhat into disuse for internal use, owing to the substitute of *Aconitum paniculatum* for the preparation of extract, and of Japanese roots not derived from *A. Napellus,* or of German roots of mixed species, for tincture, since these have not the same physiological action, and indeed, contain different alkaloids. These roots, costing half the price of good English root of *Aconitum Napellus,* have practically stopped cultivation in this country, and although during the war it has risen to a price that would pay for its cultivation, the uncertainty of the price being kept up after the war has not led to cultivation on a commercial scale.

The small quantities grown by lady herbalists since the war commenced in 1914, so far as my examination of them has gone, only in two cases proved to be genuine *A. Napellus,* so that even the small amount of "English aconite" in commerce at present is of doubtful origin. Fortunately homœopathists in this country are more careful to secure the genuine species and a definite variety of it, and by preparing the tincture from the fresh plant collected in May, when the characters that distinguish the flower can be seen, their "mother" tincture can generally be depended upon to give promptly the physiological action of the plant. I would suggest that in the next pharmacopœia the tincture of *Aconitum Napellus* should be prepared from the fresh plant, collected in May and grown in Great Britain. This would exclude nearly all the other species grown in gardens, since they flower later, and the plant if collected as soon as the flowers begin to expand would show the shallow helmet characteristic of the best form of *A. Napellus.*

BOOK REVIEWS.

SQUIBB'S ATLAS OF THE OFFICIAL DRUGS, by William Mansfield, A.M., Phar.D. Published by E. R. Squibb & Sons, New York, N. Y.

While recognizing the fact that this book has been prepared and distributed to a large extent as a means of advertising the products of a pharmaceutical manufacturing house, we appreciate also that in this publication a distinct service has been performed to pharmacy. A working knowledge of drugs is far too limited among those whose duty it is to supply medicines and who should be well equipped with such information. Any work that will encourage the study of pharmacognosy and stimulate the pharmacists and the students of pharmacy to acquire a more intimate and accurate knowledge of the materia medica is a welcome addition to the pharmacist's library and this book is well calculated to render such a service.

The intent of the author to present in a practical manner what he terms "the living materia medica, the standardized drugs of the United States Pharmacopœia and of the National Formulary" is well carried out. We cannot, however, refrain from criticizing the language of this statement as there are many articles of materia

medica which from the frequency of use are surely "living materia medica" that are not included in the present editions of either the U. S. P. or N. F. Moreover, these official promulgations have "standardized" comparatively few of the official drugs of vegetable or animal origin, in that their therapeutic activity is determined by chemical assay of their active medicinal constituents or by a physiological assay of their potency.

While agreeing with the statement in the preface that "all that is mentioned in Squibb's Atlas is of worth," we are not prepared to endorse the initial laudatory statement therein that "Squibb's Atlas of the Official Drugs is a complete, up-to-date, trustworthy handbook on pharmacognosy." As a matter of fact, "a complete, up-to-date and trustworthy handbook on pharmacognosy" has not yet been published in the English language.

The classification of the contents is simple and excellent and the treatment of the macroscopic characters of the materia medica considered is concise, to the point and in the main quite satisfactory. The terms used in the descriptions are necessarily technical, but are free from the ultra scientific phraseology that has too frequently confused the students of pharmacognosy. "Hackly" is a good English word and well selected to define "a fracture with a sharp and jagged surface." We note, however, that in speaking of fracture on page 9 the word *"concordal"* is used, instead of *conchoidal,* to define a fracture with curved surface and that in numerous other places throughout the pages the same error occurs.

The photographic illustrations of crude drugs and of trade or imported packages of some of these, are good pictures of type specimens as the drugs should appear in commerce. These pictures are the most valuable feature of the book and generally well represent the macroscopic appearances. As a means of presenting the histological characteristics, these illustrations cannot be looked upon as a success. For example, the size of the pictures of the cross sections of Mexican sarsaparilla and of triticum preclude anything like a differentiation of the tissues present in these. Modern pharmacognosy is concerned equally with the study of the microscopic as well as the macroscopic characteristics of drugs as a clear understanding of both is essential.

G. M. B.

AN ADVANCED COURSE IN QUANTITATIVE ANALYSIS WITH EXPLANATORY NOTES, by Henry Fay, Ph.D., D.Sc., Professor of Analytical Chemistry in the Massachusetts Institute of Technology. First Edition, v + 11 pages. New York, John Wiley and Sons, Inc.; London, Chapman and Hall, Ltd. Cloth, $1.25 net.

Intended primarily for students of the above mentioned institution who have finished the introductory course in "Qualitative Analysis," the title unfortunately does not enable one to judge the contents which are as follows:

Part I—Mineral Analysis:

Sampling for Analysis; Determination of Silica in Decomposable and Refractory Silicates, of Potassium and Sodium in Silicates; Analysis of Spathic Iron Ore; Determination of Sulphur in Pyrite, of Titanium in Titanium Iron Ore; Iodometric Determination of Copper; and Proximate Analysis of Coal.

Part II—Metal Analysis:

Phosphor-Bronze; Carbon, Manganese, Phosphorus, Sulphur, Copper, Nickel, Chromium, Tungsten, and Vanadium in Steel; Phosphorus, Sulphur and Silicon in Cast Iron.

Concluding with Tables of Atomic Weights and Logarithms (4 place) and the Index.

Methods of analysis are followed by a series of explanatory notes in which attention is directed to the reasons for prescribed procedures, to errors that are possible, to advantages which one method may have over another, to the influence of certain constituents upon the properties of metals or alloys and to literature references.

The excellent plan followed in this book could, with advantage, be used in books taking up other lines of quantitative analysis. A close inspection of the book has disclosed but few necessary corrections or suggestions. On page 28 the coefficient in the formula of water is transposed. On page 110 (index) magnesium is proper where printed, but in the text, pages 18–19, giving directions for certain manipulations, no reference is made to the fact that magnesium is being determined nor is even the composition of the final product given, except in the explanatory notes on page 27. Manganese is not given in the index, but it was found that the last two lines under magnesium related to manganese.

FRANK X. MOERK.

ESSENTIALS OF PHARMACY, by L. E. Sayre, Dean and Professor of Pharmacy and Materia Medica, and L. D. Havenhill, Professor of Pharmaceutical Chemistry, of the School of Pharmacy, University of Kansas. Cloth, 12mo, 466 pages. Published by W. D. Saunders, Philadelphia.

This publication, an enlargement of an earlier edition, consists of a concise assemblage of pharmaceutical facts. The first section deals with general processes and definitions, the official inorganic chemicals and related subjects are next considered, then the organic chemicals of the Pharmacopœia and N. F., and lastly, the pharmaceutical preparations of both books.

The facts are condensed and an effort has been made to place before the student only the most essential considerations. The arrangement is such that the chief value would seem to be for purposes of a review by students who have already been well grounded in the subjects presented, since these are presented alphabetically and without any consideration of their relation to each other. As an illustration, the unrelated subjects of "elutriation," "enfleurage," and "evaporation," follow each other because of their alphabetical order.

This book would therefore seem to find its chief use for the graduate who is reviewing the "essentials" of pharmacy, or for a student who is preparing for examinations. The typographical arrangement is excellent and the text has evidently been carefully prepared.

E. F. C.

OBITUARY.

JOHN F. PATTON.

John F. Patton, former president of the American Pharmaceutical Association, died at his home in York, Pa., on Monday evening, March 17, after only a few hours illness, his death being attributed to heart trouble. Although in his eightieth year, he had enjoyed good health and up to the day of his decease was actively engaged in his pharmacy.

John F. Patton was born in Lower Windsor Township, York County, Pa., on December 15, 1839. He was the fourth son of Ebenezer and Rebecca (Smith) Patton. His grandparents were

sturdy Irish immigrants who settled in Chester County, Pa., in 1780, and raised a family of fifteen children, twelve boys and three girls.

John F. Patton received his education in the public schools and in 1853 he came to York and engaged as a clerk in a dry goods store. In 1856, he decided to take up the study of the drug business and engaged with Dr. Jacob Hay, Sr. From 1859 to 1866 he was in the employ of the wholesale drug firm of Thomsen & Block, Baltimore, Md. In 1869, he opened a small store for himself on the north side of West Market Street, York. He soon prospered and in 1873 he removed to a larger store. His efforts and ability were rewarded with a constantly increasing business and in 1884 he built a three-story brick building with what, at that time, was considered a large store. Before his new store was completed, his drug stock was almost entirely ruined by the disastrous flood in June of that year and Mr. Patton had a narrow escape from death. Up to the time of his decease, he continued in the drug business at this location and enjoyed a wide circle of friends and customers.

John F. Patton never married. He was a member of St. Paul's Lutheran Church. He was noted for his quiet, yet effective service, that won the esteem and confidence of all with whom he came in contact. He always took an active interest in the pharmaceutical organizations and for many years faithfully attended the meetings of the Pennsylvania Pharmaceutical Association and the American Pharmaceutical Association, and the appreciation of his work in behalf of his chosen profession is shown by the fact that he was elected to the presidency of the State Association in 1891, and in 1900 was elected President of the American Pharmaceutical Association and presided over the meeting of that body held at St. Louis in 1901.

JAMES OSCAR BURGE.

James Oscar Burge died at his home in Nashville, Tenn., on February 6, 1919, in his seventy-first year. He was born near Bowling Green, Kentucky, on March 27, 1848. He was graduated from the Philadelphia College of Pharmacy in 1876 with honor, having passed a meritorious examination and ranking seventh in a class containing many who subsequently won distinction in the profession of pharmacy. Among these we may mention Professors Henry Trimble and C. S. N. Hallberg. The subject of Mr. Burge's

thesis was "The Chemical Laboratory," and throughout his many years of pharmaceutical experience his preference was well known to be for chemical and laboratory work.

He engaged in the drug business in Bowling Green, Ky., and later in Nashville, being interested in a number of drugstores in these localities. In recent years he was associated with several wholesale drug and chemical companies, his most recent venture being the Gattis Chemical Co. which he organized in connection with his son, J. O. Burge, Jr.

He joined the American Pharmaceutical Association in 1878 and was elected honorary president in 1916–1917. He always took an active part in matters pharmaceutical and usually attended the meetings of the A. Ph. A. He was one of the best known pharmacists in the country as well as a leading exponent of pharmacy in Tennessee. He was the president of the Nashville Branch of the A. Ph. A.

He took an active interest in the civic matters of the city and also in the religious circles and was a member of the Edgefield Baptist Church.

DR. NATHAN C. SCHAEFFER.

Dr. Nathan C. Schaeffer, Superintendent of Public Instruction in Pennsylvania, died at his home in Lancaster, Pa., on Saturday evening, March 15, after a lingering illness, at the age of 70 years. He was born in Maxatawny Township, Berks County, Pa., on February 3, 1849. He was educated at the Franklin and Marshall College, graduating therefrom in 1867 and later received the degree of doctor of philosophy from his alma mater.

He likewise attended several of the German universities and also studied at the Theological Seminary of the Reformed Church. Dickinson College conferred upon him the degree of doctor of divinity and doctor of laws in 1904.

His literary work was mainly on educational and Biblical subjects. He was a professor at Franklin and Marshall College from 1875 to 1877, when he resigned to accept the position of principal of the Keystone State Normal School. In 1893 he was appointed State Superintendent of Public Instruction, and retained this position throughout the several administrations until the time of his decease. He was the chairman of the commission that drafted the present Pennsylvania State School Code.

PROFESSOR JOSEPH KAHN.

Professor Joseph Kahn, Phar.D., of the Brooklyn College of Pharmacy, in which he held the chair of chemistry, died suddenly at that college on March 3, and he was buried with impressive ceremony therefrom on Wednesday, March 5.

He was a Russian by birth and about forty-five years of age. Emigrating to this country as a poor immigrant lad, he succeded in obtaining an education by perseverance and a determined financial struggle. With few friends to divert his attention, he devoted himself to the study of pharmacy and later to the mastering of the chemical sciences. By the dint of his efforts he won recognition, position, and the esteem of many with whom as a teacher and member of the pharmaceutical societies he came in contact. The contributions that he had made to pharmaceutical literature evidenced his ability for research and the possibility of a bright professional career.

HENRY KOOPMAN.

Word has been received in this country of the death in Sweden on January 5 of Henry Koopman, formerly of McKesson & Robbins, and well known to retail druggists throughout the United States. Mr. Koopman joined McKesson & Robbins in 1875 and was for thirty-eight years active in the development of its business. Among some of his other activities, Mr. Koopman organized the Spanish Department of McKesson & Robbins, now one of the large flourishing departments of that organization. In April, 1913, on account of heart trouble, Mr. Koopman retired, by the advice of his physicians, and went to Sweden, the home of his wife, where he has since resided, and where, as just advised, he died.

NEWS ITEMS AND PERSONAL NOTES.

THE HARRISON NARCOTIC LAW UPHELD.—In two recent decisions the U. S. Supreme Court has sustained the constitutionality of the act approved December 17, 1914, and commonly called the Harrison Act. The first decision was based upon the case of C. T. Doremus, a Texas physician, who was accused of selling a quantity

of heroin tablets to a "dope fiend" for use as an habitual user and further that the sale was not on a written order on an official narcotic order in accordance with the provisions of the law, thereby violating sections 1 and 2 of the Act.

The contention of the defendant was that section 2 was an interference with the police powers of the states and was not related to the collection of excise taxes. By a majority decision the validity of the measure was affirmed because it opened a possible way for dealings in narcotic drugs without the payment of the revenue tax.

The second decision was based upon the case of Dr. Webb, a physician, and one Goldbaum, a druggist of Memphis, Tenn. The former prescribed morphine for the purpose of habitual use to "dope fiends" and the latter had filled over 4,000 such prescriptions; the specific case cited was a sale to a non-resident of the state of ten so-called prescriptions, at one time, for one drachm each of morphine. The decision upholds the constitutionality of the provision that the sales of these narcotic drugs must be made only on the official order forms or on registered physicians' prescriptions given in good faith in the treatment of disease or to effect a cure.

The Chief Justice and three other members of the Supreme Court dissented from these opinions.

LEHN AND FINK PROVIDE LARGER FACILITIES FOR BUSINESS.—Messrs. Lehn and Fink, Inc., the well-known wholesale druggists and manufacturing pharmacists of New York City, announce that they have completed arrangements for the erection of a new six-story building to be located at Greenwich, Morton and Barrow Streets. As soon as the new building is completed they will remove from their present location, 118–120 William Street, and their expectation is to have at least three times the space that they have available at the present time. The firm was organized in 1874 and was composed of gentlemen who had a large acquaintance with the drug trade and who were well equipped and possessed a broad knowledge of the drug markets of the world. The successful development of a line of pharmaceutical specialties contributed materially to their business growth which has necessitated the acquisition of new and larger quarters.

PRINCIPLES OF THE U. S. P. REVISION TO BE DISCUSSED.—Dr. Wortley F. Rudd, chairman of the Section on Education and Legis-

lation of the A. Ph. A., announces that it is proposed to devote a portion of one session of that Section at the New York Meeting of the association in August to a discussion of the general principles that should obtain in the next revision of the U. S. P. Constructive papers, suggestions and discussions will be the timely object in view.

THE INTER-RACIAL COUNCIL AND ITS WORK.—This organization, of which Coleman du Pont is chairman and Philip T. Dodge vice-chairman, has opened offices at 120 Broadway, New York City, and has engaged upon an important educational programme of Americanization. In a recent communication attention is directed to the importance of developing "A Foreign Market at Home." It is shown therein that there are in America fifteen million foreign-born, and including those of foreign parentage, it is estimated that there are thirty-three million who should be cultivated as purchasers of American-made wares, instead of encouraging the existing preference for the familiar production of their native countries.

The campaign is to make the thrifty foreigner a good customer for American goods; to teach him the merits of such and to encourage him to live in truly American style and ways. The purpose is to further this movement in various ways, not the least important of which will be by utilizing advertising space in the 1,146 American papers printed in foreign languages in the United States (excluding the German, which number 483) and 85 magazines, many of which have a wide circulation and exert great influence. These are to be made "trade missionaries" to aid in the Americanization plans contemplated.

CHANGES IN THE MANAGEMENT OF H. K. MULFORD CO.—At a recent meeting of the directorate, Mr. K. K. Mulford resigned as vice-president of the corporation and Mr. Hilson H. White was elected to fill this responsible position. Mr. White was born in Scotland and received his education in several colleges in Scotland and England. He was engaged for some years in one of the large pharmacies in Toronto, Canada.

Having accepted a position as a travelling salesman with the H. K. Mulford Co., he enthusiastically devoted his energies to what was to him a congenial opportunity for expansion. His success and marked ability won recognition and in 1910 he was made general sales manager for the company. Advancement has been rapid, and

in 1915 he was elected a director and in 1918 was made assistant to the president, and now has the further honor of being made vice-president.

Mr. R. L. Derr, who for some years past has been the manager of the Chicago branch of the H. K. Mulford Co., has been promoted to the position of supervisor of the various branches of the company and has removed to the home office in Philadelphia to assume charge of his new duties.

DR. A. PARKER HITCHENS WITH ELI LILLY AND COMPANY.—Dr. A. Parker Hitchens, who has a national reputation as one of America's leading bacteriologists, has accepted an appointment in the management of the Biological Laboratories of the Eli Lilly Company of Indianapolis.

Dr. Hitchens is the secretary of the American Society of Bacteriologists and is the editor of the publication of that organization *Abstract of Bacteriology*. During the war he entered the Army Medical Service and was commissioned as a major and assigned to duty in the Army Medical School in Washington and devoted most of his time to the study of the bacteriologic problems associated with influenza. Upon discharge from the active service, he was commissioned a lieutenant-colonel in the Medical Reserve Corps.

CHANGES IN THE SCIENTIFIC STAFF OF BURROUGHS WELLCOME RESEARCH LABORATORIES.—Dr. T. A. Henry, late superintendent of the laboratories at the Imperial Institute, London, has been appointed director of the Wellcome Chemical Research Laboratories, London.

Dr. F. L. Pyman, the former director of these laboratories, has accepted the professorship of technological chemistry in the Manchester Municipal College of Technology, and in the University of Manchester.

THE REMINGTON MEMORIAL HONOR MEDAL IN PHARMACY AWARDED.—The first award of the Remington Honor Medal, provided by the New York Branch of the American Pharmaceutical Association, is to be made this year. The Committee on the Award have selected Dr. James H. Beal, former president of the American Pharmaceutical Association as the first recipient of this distinguished honor.

Dr. Beal's work in behalf of pharmacy is too well known to require any recounting at the present time. As general secretary of the A. Ph. A. and as the first editor of the *Journal of the American Pharmaceutical Association,* as member and president of the National Drug Trade Conference, as chairman of the Commission on Proprietary Medicines, as chairman of the Board of Trustees of the U. S. Pharmacopœial Convention, and in many other ways has he shown his exceptional ability and his earnest efforts in behalf of the profession. The honor is deserved and the distinction accorded is fully merited.